THE

PHYSIOLOGICAL ANATOMY

AND

PHYSIOLOGY OF MAN.

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This edition of the original work of Dr. Todd and Mr. Bowman, has been prepared by Dr. Beale, their successor in the chair of Physiology and of General and Morbid Anatomy in King's College. His name therefore appears in the title page as joint author.

Dr. Beale had already assisted the authors in the completion of the concluding part of their second volume, but for the work in its new form he is alone responsible.

The present part, consisting of the *Introduction*, Chapter I. on *Structure*, and Chapter II. on *Chemical Composition*, is complete in itself. In the further prosecution of the work, the original plan will be adhered to as closely as possible, but the text will be modified where necessary, and numerous new figures introduced.

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INTRODUCTION.

THE aim of all natural knowledge is to ascertain the laws which control and regulate the phenomena of the universe. So numerous, and so diversified are these phenomena, that for their study a division of labour has been found not merely convenient, but absolutely necessary. The position and movements of the planetary system, the crust of the earth, and its various component strata, the treasures hidden in its womb, the abundant vegetation that grows upon its surface, or beneath its waters, and the numberless hosts of animals that dwell upon the land, or in the rivers, lakes, and seas form separate branches of scientific investigation, between which a sufficiently distinct line of demarcation is established by the nature of the objects of inquiry peculiar to each. But, in all departments of science, the same general rules for conducting the investigation prevail, and it is only by a close adherence to these that we can arrive at safe and satisfactory conclusions.

In any scientific inquiry, the first step must be to form a general notion of the characters and properties of the objects of investigation. In the next place, it is necessary to observe carefully the phenomena which they naturally present; and, if they be within our reach, to produce such variation in them by artificial means (by experiments), as may serve to throw

light upon their nature. If the phenomena under observation be complex, we must analyse them with a view to ascertain the simpler ones of which they are composed. By this analysis, and by the elimination of such as are merely collateral, we arrive at a phenomenon, uncomplicated, incapable of further subdivision, and fundamental; and this we are contented to receive as an *ultimate fact*, the result of a law in constant and universal operation. The accumulation of observations and experiments affords us Experience; points out the ordinary succession of phenomena, and teaches us the ways of Nature. If these phenomena are found to present a certain uniformity, we are authorized to refer them to the operation of one common Cause, and we are thus led to the expression of the Law which regulates their occurrence. Proceeding in this way, we are enabled to explain the whole train of phenomena which have been investigated,—that is, to devise a *Theory* which develops the rationale of their occurrence.

But sometimes our experiments and observations throw an imperfect light upon the phenomena which are the subjects of investigation; or the latter are so remote, or so little under our control, as to render both observation and experiment extremely difficult, and in some cases impossible. The "instances" which we are enabled to collect are, consequently, dubious and obscure, and point darkly or not at all to ultimate facts; they present little or no general resemblance, and cannot be properly associated together. Here is no foundation on which to build a theory; but great advantage may be gained, if, with the little light we derive from these particular observations, aided by previous knowledge of general laws, we can frame an *hypothesis*, offering some explanation of the phenomena. The adoption of such an hypothesis, even for a temporary purpose, will "afford us motives for searching into analogies," may suggest new modes of observation and experiment, and "may serve as a scaffold for the erection of general laws."

Previously to the time of Lavoisier, chemists were perfectly familiar with the occurrence of combustion under various circumstances; but the opinions (hypotheses) which prevailed as to the real nature of this process, afforded a very unsatisfactory explanation of it. Subsequently, however, by the labours of Lavoisier, Davy, and others, this complex phenomenon has been observed in all its phases; it has been carefully analysed, and

has been proved to occur in all cases, where substances possessed of strong chemical attractions, or different electrical relations, are brought within mutual influence. The *ultimate fact* thus arrived at is, that intense chemical combination always gives rise to the evolution of heat, and, in many instances, to that of light also.

Again, a great number of observations have shewn that bodies combine together only in certain quantities, or in multiples of them; that each body has its proper combining quantity, and that it never enters into combination except in that quantity, or some multiple of it. This is an *ultimate fact*, ascertained by numerous experiments, and indicates the law, which is so important in chemistry, that bodies unite with each other in their combining proportions only, or in multiples of them, and in no intermediate proportions. And this, again, has led to the beautiful generalization of Dalton, that the ultimate atoms of bodies are their respective combining quantities, and bear to each other the same proportion as their combining equivalents do.

Or, to take an example from the science which is to form the subject of the following pages. The function of respiration in animals is a very complex process, respecting the nature of which many unsatisfactory hypotheses had been formed, owing to the obscurity in which many of the phenomena, immediately or remotely connected with it, were involved. Until the law of the diffusion of gases, and of the permeability of membranes by them, had been developed, and until it had been shewn that carbonic acid is held in solution in venous blood, no theory of respiration could be framed adequate to explain all the phenomena. It is now proved, that, in this process, a true interchange of gases takes place through the coats of the pulmonary blood-vessels, the oxygen of the air passing through and occupying the place of the carbonic acid of the blood while the latter is diffused into the air in the pulmonary vesicles. An admirable example is thus afforded of a process most important to life taking place in obedience to a purely physical law.

Living objects are those which properly belong to the science of Physiology. These are strongly contrasted with the inanimate bodies (which have never lived), to which other branches of natural science refer. At the same time, there are many points of resemblance between them; and as both owe their

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origin to the same Divine Author, and are reducible (as will be seen by-and-by) to the same elementary constituents, so they are subject in a great degree to the same physical laws, and are to be investigated according to the same principles of philosophical inquiry.

In this Introduction we propose, in the first place, to consider the characters in which organized bodies agree with or differ from inanimate, mineral, or unorganized bodies, and then to refer briefly to the structure and special endowments of living beings. Next, the relation of the physical and vital forces will be briefly discussed, and we shall endeavour to show that physical are distinct from vital phenomena. Life and some of the theories of life of the greatest interest to the physiologist will then be alluded to, and the diversity of the forms of living beings, and the general differences existing between plants and animals considered. Lastly, we shall endeavour to point out the value of a knowledge of physiology, especially that of man, to the diagnosis and treatment of disease, and the modes of pursuing this branch of natural knowledge.

OF ORGANIZED AND UNORGANIZED BODIES.

Living beings have been sometimes said to be *organized* in the sense of being composed of certain distinct parts or *organs*, each having its own definite structure, and capable of fulfilling a certain end. But if the term be used in this sense its use must be restricted to the higher organisms after they have reached a certain stage of development, for every independent living organism, at the outset of its life, consists merely of a colourless, transparent semifluid matter, disclosing no structure whatever, and possessing no distinct parts or organs. Yet this matter lives; it is capable of formation, of increase, and of multiplication, and it must be regarded as an independent living *organism,* organized although exhibiting no structure. We therefore extend the term *organized* to every kind of matter endowed with these peculiar powers or capabilities. They are characteristic of life, and are manifested by living matter which came from pre-existing living matter: never have such endowments been shown to exist in relation with any inorganic unorganized matter whatever.

All organisms are composed of and are capable of producing peculiar organic matters of complex composition, and often endowed with peculiar properties.

By *proximate analysis* several different organic compounds may be obtained from every organism. By *ultimate analysis* these organic compounds may be resolved into simple elementary substances, such as constitute other objects of the universe.

The various bodies that compose the mineral kingdom, have not the same complex composition, nor do they exhibit that distinctness and variety of structure in their component parts, which is so characteristic of at least the higher organisms, nor is there any adaptation of their parts to separate functions. They never exhibit the wonderful properties characteristic of the living matter which exists in all organisms, but in these alone, and they are therefore called *unorganized* or *inorganic.* Chemical analysis resolves them into simple elements which admit of no further subdivision.

Life, Death, and Dormant Vitality.—Organized bodies are found in two states or conditions. The one, that of *life*, is a state of action, and of change. The other, that of *death*, is one in which all vital action has ceased, and to which the disintegration and chemical decomposition of the organized body succeed as a natural consequence. But it cannot be said that any living body exists which at any one moment consists entirely of *living matter.* In every living organism, at every moment, so long as its life lasts, there is matter that lives and matter that *has ceased to live.*

An organized body in a state of *active* life exhibits *growth* and *nutrition*, and resists the destructive influence of surrounding agents. Thus the development of structures is promoted, and the integrity of the body itself is preserved. The simplest thing growing, animal or vegetable, is an illustration of this remark.

But there are organized bodies in which life is said to be *dormant.* If in these, actions or changes occur, they are so slight that they cannot be observed; nevertheless, if placed under certain favourable conditions, vital activity will soon become manifest in these organized bodies. Of this we have familiar examples in a seed, and in an egg. It is well known that seeds will retain their form, size, and other properties for a

very considerable period; and afterwards, if placed under favourable conditions, will exhibit the process of germination as completely as if they had been only recently separated from the parent plant. Eggs, also, may be preserved for a long time without injury to the power of development, or to the nutrition of the embryo contained within them. But neither eggs nor seeds will exhibit vital activity if kept beyond a definite period of time. This fact renders it probable that certain slow changes do occur even in this dormant state; and that when these changes have once ceased no altered conditions whatever will recall the power of germination to egg or seed.

It is worthy of observation, that those processes, which denote vital activity, may be sometimes temporarily suspended, even in fully formed animals and vegetables; and, in such instances, life may be said to *become dormant*. That is, under these altered conditions, changes occur so slowly as not to be perceptible to ordinary observation. The privation of moisture or of heat is the ordinary cause of this partial cessation, or diminished activity of, the phenomena of life. In dry weather, mosses often become desiccated, and although they *appear* quite dead, will nevertheless speedily revive on the application of moisture. The common wheel animalcule, although apparently killed by the drying up of the fluid in which it had been immersed, will speedily resume its active movements on being supplied anew with water. But this desiccation is not perfect and complete desiccation. Whenever living matter of any kind is perfectly dried, it is killed, and can never be resuscitated. The manner in which the living matter is protected renders it very difficult to dry it thoroughly, and if but the *most minute particle* remains moist, it may retain its vitality, and increase and exhibit vital actions whenever the conditions under which it is placed become favourable. Certain living organisms and tissues may be frozen without being killed, but in this case it is doubtful if the germinal or living matter itself be rendered solid, any more than by desiccation it is completely deprived of water.

Composition of Organized and Unorganized Bodies.—Inorganic bodies may be resolved by ultimate analysis into oxygen, hydrogen, nitrogen, carbon, and about fifty other substances, which chemists regard as simple, because they appear to consist of one kind of matter only; that is to say, they have hitherto

resisted futher dceomposition. These elements unite in certain definite proportions to form the compound inorganic substanccs.

Organized bodies are capable of being resolved, by *ultimate analysis*, into inorganic simple clements; but the list of simple substances which may be obtained from this source compriscs only about twenty. Of the four widely-spread elements, oxygen, hydrogen, nitrogen, and carbon, two, *at least*, will be found in every organic eompound; henee, as Dr Prout has suggested, these four may be eonveniently distinguished as the *essential* elements of organic matter. The other simple substances are found in smaller quantities, and are less extcnsively diffused; these may be termed its *incidental* elemcnts. They are sulphur, phosphorus, chlorine, sodium, potassium, ealeium, magnesium, silicon, aluminium, iron, manganese, iodine, and bromine, and probably others; the last two are obtained almost exelusively from marine plants and animals.

Proximate Principles.—From various animal and vegetable tissues, and from their fluids, may be obtaincd by proximate analysis, a class of substances which have been grouped together under the head of *proximate principles*, or *organizable substances*, because they are specially eoneerned in nutrition. It is these substances which form the most important constituents of the *food* of man and the higher animals. The following are examples of proximate principles—*gluten*, *starch*, *lignine*, from the vegetable texturcs; *albumen*, *fibrine*, *casein*, from the animal ones. From the organized structure, called *muscle*, for example, we obtain by *analysis*, first *fibrine*, a proximate prineiple, which is its chief constituent; and, subsequently, by the analysis of fibrine, we get the *simple elements*, oxygen, hydrogen, carbon, nitrogen, and sulphur, in eertain proportions. On thc other hand, by *synthesis*, or the combination of certain simple inorganic elements in the organism of the plant, an organic eompound, closely allied to fibrine, is produced; from whieh, or from allied substances forming the food of animals, the organized strueture, muscle, is formed.

In many *organized bodics* thc constituent particles are, as it were, artfully arranged, so as to form peeuliar *textures*, destined to serve special purposes in the living meehanism of the animal or plant to which they belong. These textures exhibit peeuliar *structurc*, which is one of thc results of vital action, although

the *tissue* which has been formed may not be alive. The chemical compounds which may be obtained from these textures by analysis are devoid of any mechanical arrangement of particles.

From these again a great variety of compounds has been obtained by various chemical processes, owing to the tendency which their elements have to form new combinations. By boiling starch in dilute acids, it becomes converted into a kind of gum, and starch-sugar; and, in the germination of barley, or of the potato, a peculiar substance is formed, the contact of which with the starch of the barley or potato converts it into sugar. Innumerable examples might be quoted from various vegetable compounds, shewing that the affinity, which holds together the elements of organic substances, is so feeble, that it affords but slight resistance to their entrance into new combinations.

The proximate principles of organic substances consist for the most part of three or four of the essential simple elements, and, as many of them contain a large number of atoms, their combining proportion is represented by a very high number. Respecting the mode of combination of these elements however, the greatest uncertainty prevails, and it is indeed doubtful if many of the substances which have received special names, as *albumen*, *fibrine*, and the like, are really definite chemical substances of fixed composition. Chemists have not yet succeeded in obtaining the majority of these bodies in a state of chemical purity.

Secondary Organic Compounds.—From the blood, from the tissues, and from many of the fluids secreted by different organs of the body, by *proximate analysis*, may be obtained another class of substances derived from the process of *destruction* of the organic substances entering into the formation of the tissues, blood corpuscles, or gland cells. These have been called secondary organic compounds, and their chemical composition is far simpler than that of the proximate principles. *Urea*, *uric acid*, *kreatin*, *kreatinine*, *hippuric acid*, *leucin*, *tyrosin*, are all organic substances, which result from the oxidation and disintegration of more highly complex organic substances in the organism, and are examples of secondary organic compounds.

Of the Synthesis of Organic Compounds.—As has been remarked already, much uncertainty exists in reference to the manner of combination of the simple elements to form the higher and more

complex organic compounds. It is therefore not surprising that the attempts of chemists to produce them by artificial processes should have met with so little success. No one has succeeded in the formation by synthesis of albumen, fibrine, or any of those substances (as for example, the constituent of white fibrous tissue), of which the greater part of the bodies of animals is composed. Not even starch, or the cellulose of the very lowest simplest vegetable organisms has been prepared by synthesis in the laboratory. Indeed, it is very questionable whether any of those substances which may be considered as the first or immediate result of *vital actions* will ever be produced elsewhere than in the living organism.

Of late years a vast number of those substances which result from the action of oxygen upon compounds formed in animal and vegetable organisms have been made in the laboratory from inorganic matter. The formation of urea, a *secondary organic compound*, has been effected by Wöhler from the cyanate of ammonia, by depriving it of a little ammonia through the action of heat. And it must be admitted, as no unimportant step in the synthesis of organic compounds, that nitrogen gas has been found to unite with charcoal, under the influence of carbonate of potassa at a red heat. The cyanide of potassium, which is thus formed, yields ammonia, when decomposed by water; so that cyanogen, and through cyanogen, ammonia, can be primarily derived from their respective elements contained in the inorganic world. Allantoin, an analogous compound to urea, formic, oxalic, glycolic, lactic, butyric, leucic, oleic, and a number of other organic acids, have likewise been artificially produced. No compound allied to albumen has yet been prepared artificially, but many substances bearing to it much the same relation as urea, have been produced. In short, the substances already formed in the laboratory by synthesis, correspond with those which are produced by the chemical action of oxygen upon products resulting from the disintegration of more complex chemical substances. They are allied rather to the substances included in the secondary compounds, than to the group of proximate principles. They are the results of a long series of chemical changes occurring in the organism, and are so far removed from the actual constituents of the tissues, and from the substances which immediately result from the death of

living matter, that their artificial production affords no safe grounds for supposing that the former complex substances will ever be manufactured in the laboratory, or that a living organism will some day be produced by the synthesis of inorganic elements as some have not hesitated to regard as possible when organic chemistry shall have advanced to a higher state of perfection.

OF THE STRUCTURE AND SPECIAL CHARACTERS OF ORGANIZED BEINGS.

The *higher plants and animals* are composed of parts often termed organs, distinct from each other in structure and function. Entering into the formation of these organs are many different textures, each differing from the others in physical properties, in their mode of action, and in chemical composition. The existence of a great variety of textures in an animal implies a high degree of organization.

In *beings of a more simple character*, low in the scale of organization, there is comparative uniformity of structure; though often a variety of parts or organs, and tissues having different properties, exist in the fully developed organism. But, in many cases, it has been observed, that from almost any one part of the body any other portion might be developed. Thus some species of Actinia, in slowly moving over the surface of a rock, detach small pieces of the margin of the disc. From each one of these detached portions a perfect actinia, with its tentacles, external covering, gastric membrane, glands, and muscular and nervous apparatus and generative organs, is developed.

In the *lowest and simplest organisms* there is no indication of distinct parts or organs. The entire creature seems to consist only of a small mass of clear structureless material, which possesses in every part the power of moving in any direction, which absorbs nutrient matter, and grows and multiplies by portions being from time to time detached.

There is a time when every organism, even the most complex, consists of such a simple mass of colourless, growing, moving, matter. Every organ, every tissue, is represented at an early period of its development by such a simple and apparently almost homogeneous mass of plastic material. Such structureless material exists also at every period of the life even of the most complex tissues. The physical property of

the tissue does not depend upon this matter, nor is its funetion due to it; but no tissue ean be produeed or be inereased without it. There can be no *life* in the absence of this simple matter. In fact, the *tissue* does not grow of itself, but new tissue is produeed by changes occurring in this soft, plastie matter, and it is added to the tissue which already exists. Neither does *the tissue* multiply, assimilate, form, or eonvert, but all these phenomena are effeeted by the agency of this wonderful *simple plastic matter*. It is remarkable, that as soon as this matter undergoes eonversion into tissue or into any definite chemical compound it loses for ever the active powers above referred to.

From this colourless transparent material, then, everything eharacteristic of a living body is formed, or, in other words, the matter of whieh all the tissues and substanees peeuliar to the organism are eomposed, was once in this state.

A mass of any tissue at every age may be divided into *elementary parts*, each one of which eontains a portion of this transparent matter within it. Each one of these elementary parts may be termed a "*cell*." In some tissues the "cells" can be readily separated from one another, but in others, the outer part or tissue of one "eell" is eontinuous with that of neighbouring cells. Various forms of eells are represented in Plates I, II, III, and IV, an examination of whieh will enable the reader to form a elear notion of the structure of the principal kinds.

The simplest or most elementary organie form with which we are acquainted eonsists of a portion of this soft, transparent, eolourless matter, surrounded by a layer of matter formed from it, which may be so thin as to be hardly visible. This latter results, in fact, from the aetion of external conditions upon the most external portion of the mass. Such an elementary part may be less than the $\frac{1}{100000}$ of an ineh in diameter, and may, we believe, exist so small as to be invisible. Still it is a living, and, in a eertain sense, independent organism, capable of increase and endowed with the power of giving rise to other bodies like itself. These wonderful powers, as already stated, reside not in the *formed* matter upon the surfaee, but in that within, whieh is in a *formless* but *living* state. The latter may be termed *Germinal matter*.

Such is the simple structure of the "cell"—of every cell which

exists in nature at an early period of its development. Remarkable alterations in character often occur as the cell advances in age, and many very different forms of "cells" result. The nature of these differences cannot be discussed here, but they will be explained when the structure of the various tissues is considered and their development traced. The account here given of the structure and action of the cell differs from that generally received in several essential particulars, but these differences will be noticed in their proper place.

Each organized body has its appropriate and specific shape; and to each a certain size is assigned. To observe and classify the wonderful diversity of forms of plants and animals, has given employment to Naturalists in all ages; and the sciences of Zoology and systematic Botany have been founded upon the results of their labours.

Every organized body, and every part of an organized body, is limited in its duration; it has "its time to be born and its time to die," and at death it passes by decomposition into simpler and more stable combinations of the inorganic elements. Death, however, occurs at every period of the life of an organized body. From what has just been remarked with regard to structure, it follows, that every anatomical element or cell is gradually undergoing change during life. Pabulum passes into the active matter and assumes the active state, while some of the latter becomes passive and is converted into new substance, which is added to that which was already formed, or takes the place of that which has been removed.

It is, therefore, evident, that not even the most minute cell is at any moment composed of matter in precisely the same state in every part. There is matter which is about to live, matter that is alive, matter which has ceased to live, and matter that is undergoing disintegration and is about to be cast away. The *entire cell* or elementary part is not alive. The inner matter is living—the outer formed matter has ceased to live. The inner matter alone is capable of growth, of germination. It may, therefore, be called living or germinal matter in contradistinction to the passive formed matter which envelopes it.

As each organized body has a certain end to serve in the economy of the living world, so each organ has its proper use in the animal or plant. In this adaptation of parts to the per-

formance of certain functions, we see the strongest evidence of Design; and, amidst much apparent difference of form and obvious diversity of purpose, the anatomist recognizes a remarkable unity of plan—affording incontestable proof that the whole was devised by One Mind, infinite in wisdom, unlimited in resource.

Of the Functions.—The various processes by which are effected the ceaseless motion and changes so characteristic of living beings, are called in Physiological language, *functions.* The function is the work, or duty, or office in the economy performed or discharged by a particular tissue or organ. Contraction is the function of muscle; the secretion of bile is the function discharged by the liver; the secretion of urine that of the kidney. Digestion, or the operation of dissolving the food, is the function of the stomach, &c. The functions may be divided into two great classes: 1. *The vegetative functions;* and 2. *The animal functions.* The first class may be further subdivided into the *nutritive functions* which are connected with the preservation of the individual; and the function of generation, which is concerned in the propagation of the species. The functions specially characteristic of man and the higher animals are locomotion and innervation. They have been termed the animal functions—a definition which is not strictly accurate, but, nevertheless, practically advantageous.

Physical processes occurring in cells. Of Diffusion. Osmose, and of the Colloid state.—Physical changes of the utmost importance occur in connection with the various processes taking place in the elementary parts or cells of living organisms. By diffusion is understood the tendency which one fluid or gas manifests to mix intimately with another. Even if the specific gravity of a fluid below be far higher than that of one which is above, the latter will gradually pass upwards and the former downwards until they are equally diffused through, and intimately mixed with, each other. This tendency, therefore, does not depend upon specific gravity, but upon some peculiar properties of the matter itself. A solution of common salt has a diffusive power nearly twenty times as great as a solution of albumen of equal strength.

Closely related to the physical process of *diffusion* is *osmose,* in which the two fluids or gases are separated from one another

by a porous diaphragm, and the result is influenced by the different degrees of adhesion exerted by the fluids or gases to the septum. Dutrochet, who first studied this process, showed that if a little alcohol were placed above a piece of bladder tied over the extremity of a funnel connected with a long tube, while the under surface of the bladder were allowed to touch the surface of water, the water, owing to its greater power of wetting the bladder, would enter into its pores, and thus pass upwards into the alcohol. This process continuing, the mixture of water and alcohol would gradually rise in the tube against the force of gravity, and would at last overflow. Here *endosmose*, the flowing inwards, of the water, greatly exceeds *exosmose*, the flowing outwards, of the spirit. The phenomena concerned in the process have been investigated by Graham, who has shown that alkaline solutions exhibit a remarkable *endosmotic* power (positive osmose), while acids exhibit the contrary, or *exosmotic* tendency (negative osmose).

In cells, and in various secreting organs, we have not only the most favourable conditions for osmose and diffusion but the means for maintaining these conditions. The process never comes to a standstill, as in our osmometers, because new acid or alkaline fluid is continually being generated to take the place of that which is removed, while the mixed and altered fluids are carried away. There is also provision for the preservation of the integrity of the porous septum, and for its reproduction.

By the recent researches of Professor Graham many very interesting points with reference to the physical constitution of several substances entering into the formation of the living body have been brought to light. He has shown that substances exist in the organism in what is termed a *colloid state*, in which condition they will not permeate a porous diaphragm; while, on the other hand, crystalloid substances will readily pass through such a diaphragm when in a state of solution in water. The fact is one of great practical importance, and has been most successfully employed for the purpose of separating poisonous matters of a crystalloid nature from their solution in the animal fluids (dialysis). The crystalloids readily diffuse themselves through a large quantity of water, while the diffusive tendency of colloids is very low.

It might be said, that the "living matter" of the cell in

which such wonderful powers are supposed to reside is simply matter in a colloid state, and it may be admitted that some of the phenomena which have been observed in connection with this matter result from or are determined by its mere physical constitution. But living matter does not possess the same properties or powers in every part of its mass, and when magnified very highly, it is seen to be eomposed of spherieal particles, varying somewhat in size. Colloidal matter, on the other hand, exhibits no such peculiarities, so that there is a great visible difference to be *observed* between this living matter and matter in a colloid state,—to say nothing of the changes occurring in the living matter, which distinguish it in the most marked manner from matter in every other known state.

Professor Graham has shown that certain *mineral* substanees exist in a colloid as well as crystalloid form. Hydrated silicic acid and soluble alumina are examples. Perhaps the most interesting example in the living organism of an organic body, which may exist in both conditions, is the material of which the red blood corpusele is composed, which sometimes, as in the case of the Guinea-pig, passes from the colloid to the crystalloid condition soon after it has been removed from the circulation and allowed to become stationary.

Of Assimilation and Excretion.—Organized bodies can appropriate and assimilate to their own textures other substances, whether inorganic or organie. This process is that which is most characteristic of living ereatures: in virtue of it, animals and plants are continually adding to their textures new matter, by which they are nourished. Plants appropriate their nutriment from the inorganic kingdom, as well as from decaying organic matter; animals, chiefly from organic matters, whcther animal or vegetable. Both possess the wonderful power of rearranging the constituents of these substances into forms identical with those of the elements of their various tissues—and of thus making them part and parcel of themselves.

Together with a proeess of supply, there is one of waste continually in operation. Animals and plants are ever throwing off effete particles from their organisms. These, under the name of *excretions*, appear in various forms—either as inorganie compounds, or as secondary organic products. Thus carbonic acid is given off in large quantities from animals; water, like-

wise, forms a considerable portion of their excreted matter, and serves to hold in solution salts, and secondary organic compounds, which result from the waste of the tissues. In this way, also, urea, uric acid, and biliary matters are excreted. In plants, water is excreted from the leaves, a phenomenon which has been compared to the perspiration of animals; and various other exeretions, which are sometimes made to serve an additional purpose in the economy of the vegetable, besides that of getting rid of superfluous matter, are doubtless formed by the secondary combinations of the effete particles of their textures.

These two processes, *excretion*, or the expulsion of effete particles, and *assimilation* of substances from without, are necessarily mutually dependent. The *work* performed depends upon the destruction of particles whose place must be occupied by new ones, for were exeretion alone to go on, the destruction of the organism must speedily ensue, by the gradual waste of the tissues; and as long as new matter is being appropriated, old partieles must be thrown off, otherwise growth would be unlimited. In both processes new eombinations are taking place, as it were, in opposite directions; in the one from the simple to the complex to form organized parts, in the other, from the complex constituents of the textures to the simple organic, or inorganic compounds.

Origin. Reproduction.—Organized bodies are always derived from similar ones. Some have supposed that out of decaying vegetable or animal matter minute animals or plants of other kinds may be formed: but it is most probable that in those cases in which they had been supposed to be formed, the seeds or eggs, or even the new beings themselves, had been concealed in the decaying matter, or eonveyed to it from the surrounding atmosphere. Neither vegetation nor the development of animalculæ will go on in fluids which have been subjected to such processes as must inevitably kill whatever germs may have been diffused around or throughout them. Every year new facts are discovered which add to the overwhelming evidence in favour of the Harveian maxim, "Omne vivum ex ovo," using here the word *ovum* in the wide sense of a germinal element derived from a parent. The progress of Anatomical knowledge is every day revealing to us the mode of generation

in the minutest and the least conspicuous forms of vegetable and animal life; and thus the hypothesis, which assumes that living objects may arise by a sort of conjunction of the inorganic elements of decomposing organic matter, becomes more and more untenable.

Of Spontaneous Generation or Heterogenesis.—Of late years the doctrine of spontaneous generation has been revived in more than one form, but, the conclusions in favour of such an origin of living beings are unsupported by sufficient evidence. Nor would it be possible were our highest magnifying powers increased tenfold, or even a hundred, or a thousand fold, to *see* the actual particles of matter combining to form part of a living structure. Those who assert that they have *seen* particles aggregating together to form a living being profess to have actually observed by a comparatively low power that which certainly cannot be seen under a power magnifying ten times more, and with advantages of demonstration which were not at their disposal.

Observations made by the use of the highest magnifying powers, and great improvements in the means of investigation not only render the doctrine of spontaneous generation less and less tenable, but demonstrate the origin of living beings from pre-existing ones in so many instances that the most sceptical ought to be convinced "that every living particle comes from a pre-existing living particle," "Omne vivum e vivo."

How beautiful is the provision which this power, possessed by organized bodies, of generating others, affords, for preserving a perpetual succession of living beings over the globe! The command, "Increase and multiply," has never ceased to be fulfilled from the moment it was uttered. Every hour, nay, every minute, brings into being countless myriads of plants and animals, to supply in lavish profusion the havoc which death is continually making; and it is impossible to suppose that the earth can cease to be in this way replenished, until the same Almighty Power, that gave the command, shall see fit to oppose some obstacle to its fulfilment.

In addition to this power of propagation, organized bodies enjoy one of conservation and reproduction of parts. Solutions of continuity, the loss of particular textures, whether resulting from injury or from disease, can be repaired. Parts,

that have been removed, may be restored by a process of growth in the plant or animal, and in some animals the reproductive power is so energetic, that if an individual be divided, each segment will become a perfect being. This power of reproduction is greater, the more simple the structure of the organized body; the more similar to each other are the constituent parts, the more easy will reproduction be. Numerous examples of this power may be adduced, — the healing of wounds, the adhesion of divided parts are familiar to every one. New individuals are developed from the cutting of plants: the division of the hydra into two, gives rise to the production of two new individuals. If a Planaria be cut into eight or ten parts, according to Dugès, each part will assume an independent existence.

The power of reproducing single parts only, is possessed by animals higher in the scale. In snails, part of the head, with the antennæ, may be reproduced, provided the section have been made so as not to injure the cerebral ganglion. Crabs and lobsters can regenerate their claws, when the separation has taken place at an articulation; and spiders enjoy the same power. In lizards, the tail, or a limb, can be restored, and in salamanders the same phenomenon has been frequently witnessed; and even in man certain tissues may be reproduced.

In the reproduction of lost parts, it must be borne in mind that changes precisely similar to those which take place during the development of the textures in the embryo, occur; in fact, the new tissues are developed from amorphous living matter. In all cases masses of simple structureless germinal matter exist, and grow, and multiply before any form or structure is manifested.

Of Putrefaction.—Dead organized matter is speedily dissipated under certain conditions. These are the presence of air, moisture, and a certain temperature, or contact with an organic substance which is itself undergoing decomposition. The conditions under which the integrity of the organic substance was preserved, have become altered, it is destroyed, and its elements are set free to obey new affinities and form new compounds.

When we consider the large number of equivalents which enter into the formation of each molecule of organic compounds, it need not excite surprise that a great variety of products results from the decomposition of animal and vegetable matter.

This decomposition is usually accompanied by *fermentation* or *putrefaction*. It used to be supposed that these were purely chemical changes, due to what was considered catalytic action, but it is now known that in both processes living organisms play a most essential part. The process of *fermentation* is dependent upon the growth and multiplication of vegetable organisms, and it is probable that the carbonic acid and alcohol so characteristic of one kind of fermentation result from the death of living particles under the conditions present. In the process of putrefaction, the researches of Pasteur have shown that so far from oxygen being necessary to the life of the simple living beings concerned, there are certain forms of infusoria which not only pass their lives without oxygen, but are killed by its presence.

All experiments have proved that the germs from which these organisms are developed gain entrance from without. The size and transparency of some of these particles are such that they are only just visible by an exceedingly good power which magnifies upwards of 5,000 diameters.* It is certain that germs exist far more minute than these. They may even exist in the interior of the higher organisms. We know they are present in great number on the surfaces of mucous membranes, and even in the interior of glands. It is probable that such germs exist in the blood, and would multiply rapidly if the state of the fluid once became favourable. Nor are cases wanting in which the decomposition of tissues, and of the blood, and the multiplication of such low forms of life, have occurred in the living body itself,—the change of course being soon followed by death. The matter, however, which is the seat of this change is dead. The life of the tissue does not become the life of the infusoria, as some have maintained, but the tissue becomes disintegrated, and the infusoria, derived from infusoria that lived before them, live upon the products, just as other organisms may live upon the matters resulting from the death of the infusoria. Living matter never lives upon living matter by the life of one organism being converted into the life of another, as some have speculated. Living matter must itself die ere it can pass as food to form part of any living organism.

* How to work with the Microscope, 3rd edit., p. 217.

In form, in size, in duration, the contrast between organized bodies and inorganic substances is most striking. The inorganic matters are aëriform, liquid, or solid: they are prone to assume the crystalline form, and to exhibit surfaces bounded by right lines, and uniting to form angles. No distinction of parts, or organs, is to be found in the mineral substance; its minutest fragment is in every respect of the same nature with the largest mass. A portion of sand not weighing a grain contains particles of the same form and size as those of the largest sand-banks known. Inorganic substances, as compared with organic, are unlimited in size and duration. Their bulk is indefinite and they retain the same condition for ages, without augmentation or waste, provided no external agent be brought to act upon them. None of those internal actions or processes, which have been described in the organized body, occur in the unorganised one; there is no inherent motion, no power of reproducing lost or injured parts, no growth, no excretion, no conversion, no formation of substances which did not exist before, no generation. From age to age the mineral remains unchanged, obedient only to the common laws of matter, and unable to modify their operation by any inherent power.

OF FORCE.

Correlation of Forces.—Force, which is constantly associated with matter in all its states, is as indestructible as the matter itself. The state or condition of the matter may be changed, but matter cannot be *generated* or *annihilated*. In like manner the form or mode of force may be altered in such a way that one form of force, as motion, may be converted into another, as heat, electricity, chemical affinity, and the like, and either of the latter may be made to resume the form of simple energy or motion. It is probable that all the physical forces are mutually convertible, but it is certain that force cannot be *produced anew* or *annihilated.*

Gravitation, Elasticity, Cohesion, Adhesion, Heat, Electricity, Magnetism, Light, Chemical action, are different forms or modes of one and the same force. The labours of Helmholtz, Grove, Mayer, and others, have proved conclusively the mutual relation, or "*correlation*," of the physical forces. Just as very different quantities of different kinds of matter represent, or are equivalent to

one another in combination, so it has been conclusively proved that one kind of force gives rise to an equal quantity of the same kind of force which produced it, or to an equivalent amount, which is constant, of some other kind of force. The exact amount of heat produced by the conversion of motion into heat has been estimated, and the mechanical equivalent of heat has been determined by the labours of Mr. Joule. A certain fixed amount of heat is always set free by the same mechanical action, lasting for the same period of time. The "motion" becomes the "heat." So the chemical combination of certain equivalent quantities of elementary substances is equivalent to the force of gravitation by which a certain quantity of matter is attracted towards, or tends to combine mechanically with other matter according to its mass; and in this mechanical combination a definite amount of heat is produced at the moment of the mechanical contact. What was *motion* is now *heat.*

The same laws apply to the physical phenomena occurring in the living organism. Chemical combination there becomes converted into heat, and the latter into motion. The amount of *work* performed by the muscles is probably due to chemical change, and particularly to oxidation occurring in the nervous system. This mechanical action of the muscle, there can be no doubt, is one of the sources of animal heat. But it must not be forgotten that a far greater amount of *work* results from the same amount of chemical change in the animal economy than can be obtained by any known machinery. The wasted force in the most perfect mechanical instrument is far greater than the force which results in actual work. In muscular action, on the other hand, we have an actual amount of work performed, which seems perfectly marvellous, when the very small weight of the machinery and the very small amount of chemical change required to keep it in action are considered. Still there can be no doubt that muscular contraction is a physical process, although physiologists have hitherto failed in their endeavours to ascertain the precise nature of the change which occurs.

Relation of Physical Forces to Vital Power.—It has been said that there exists not only a correlation between the physical forces themselves, but between the *vital* and *physical* forces. The forces, however, which have been denominated *vital* by

those who take this view, are really only physical forces manifested in living things. The sun is the source of all the physical forces operating in living beings. Living plants collect or absorb this force, and store it up in the various substances which are produced in their organisms. These, in their turn, become the food of animals, and thus the solar energy in the form of light and heat and chemical rays collected by plants, and retained by them in a quiescent state in the form of chemical combination, again becomes resolved into mechanical and other forces in the animal, and is the source of those active movements which distinguish animals from vegetables in such a remarkable degree. All the work performed by our muscles, all the heat developed in our bodies—all the chemical actions resulting from the union of oxygen with carbon, hydrogen, and other substances in the animal body, have their original source in solar energy.

Nor is it surprising, that many who have studied these matters should have fallen into the error of concluding that *life* itself was but another mode of force; and although this inference has been carefully avoided by Helmholtz and Mayer, and some other philosophers, many have expressed themselves as if they considered that we might for *life* substitute *solar energy*, *heat*, or *motion*.

Although there are some authorities who would not hesitate to affirm that every plant and animal is the mere result of changes in matter brought about by solar energy alone, it cannot be, even in a very loose sense, affirmed that a watch or a steam-engine was formed or built by the sun. And yet, to the physiologist, what poor imperfect contrivances the latter must seem, for, in spite of all the mighty human efforts required for their production, they cannot even repair themselves, much less perpetuate their race!

Hitherto not the slightest approach towards the formation by artificial means of anything having the properties of the lowest and simplest form of living matter has been made. Between the living laboratory and the chemists' laboratory there is scarcely any real analogy, for the former builds itself, and the elements therein appear to place themselves in the exact positions required for the production of the particular substance which is to be formed. This self-constructing, self-maintaining,

and self-propagating power, is referred to a something which is certainly but temporarily associated with the matter that exhibits it, and which seems totally distinct from ordinary force, since it compels the elements to take up the required special relations. The something to the influence of which all these apparently spontaneous operations is due, may be termed *vital power*.

OF LIFE.

Within every living organism, and within every elementary part or cell, are ceaseless motion and change. The absorption of new lifeless material, its conversion into living matter, the removal of that which has ceased to live, comprise a continual succession of actions in which organization and disorganization—life and death—are unceasing. But in these actions are comprised phenomena of two distinct classes, different in their very nature—*physical* phenomena, which also occur in the external world; and phenomena truly *vital*, the nature of which is not to be so explained. The *spontaneity* of the actions of the *living* structure, its self-formation and its power of multiplication, distinguish the simplest organism from the most perfect mechanism of human construction.

Life cannot be manifested without the co-operation of matter and the physical forces, but it does not therefore follow, as some have maintained, that the physical force, any more than the matter with which it is associated, is the *life*. Nor do heat, light, chemical affinity, &c., *evoke*, *excite*, or *increase* vital action, but they only accelerate certain physical changes in the lifeless matter which surrounds and protects the living matter that is within (Plates I and II), in consequence of which the passage of the nutrient pabulum through this protecting envelope, and its access therefore to the living matter are greatly accelerated. In this way the influence of heat and moisture in promoting the development of seeds maybe most easily explained.

Again, the LIFE of a complex organism, as usually defined, is made up of phenomena much more complex than those exhibited in the LIFE of a single "cell." Instead of commencing the discussion by referring to the changes which take place in the most simple living organism in the simplest condition of its existence, some observers, and especially physicists, have passed

at once to the consideration of the phenomena as they occur in a fully developed animal, or more generally in man himself. As would be supposed, the utmost confusion has resulted. The terms *physical* and *vital* have been used indiscriminately, and, gradually, many seem to have convinced themselves that *all* the changes occurring in living beings are physical.

It is not to be wondered at, that those who have taken up a view so obviously opposed to broad facts as this is, should have refrained from attempting to discuss in detail the changes which occur in a single cell; or that by some, the existence of the processes of formation, growth, and multiplication, as they take place in all living matter, has been almost ignored. These are truly vital phenomena, and occur in living beings only, but the development of heat, light, electricity, and the like, are physical phenomena, whether they occur in living organisms or in inanimate matter. Strange to say, the latter phenomena have been called *vital* when they occur in living beings, *physical* when they take place in the inanimate world; but, as they are essentially the same in all cases, it is obvious that the same terms should be applied to them. The living or germinal matter alone is the seat of *vital actions*, while in the lifeless *formed material* physical and chemical phenomena only are in operation. (See Figs. in Plates I to IV).

Matter derives *vital* powers or properties in all instances from a previously existing organism. The vital part of the impregnated egg consists of living matter, which results from living matter belonging to the organisms of the beings that produced it. It manifests a life independent of that of its parents, and undergoes development if the requisite physical conditions are supplied. Thus is life in its mysterious association with matter transmitted from one living being to another; and the life of a present generation of animals and plants has its source in that of a previous generation.

From a very early period in the history of natural science, there has been a tendency to ascribe these effects to an imaginary principle, or Entity, possessing powers and properties which (however men may try to impress themselves with a contrary notion) would entitle it to rank as an intelligent agent. It is true, that, according to most of the advocates of this doctrine, this power is supposed to be superintended and controlled by

the Deity himself, and, by this supposition, they have screened themselves against the accusation of attributing to a creature the powers of the Creator.

A little examination of this doctrine will shew that it has no pretensions to the title of a theory.

Aristotle attributed the organization of animals and vegetables, and the vital actions exhibited by them, to a series of *animating principles* (ψυχαι), differing according to the nature of the organized bodies constructed by them, and acting under the direction of the Supreme animating principle (φυσις). He supposed that each particular kind of organized body had its proper animating principle or ψυχη, and that the variety of the former really depended upon certain original differences in the nature of the latter, so that every distinct species of animating principle would necessarily have its appropriate species of body.

Harvey, likewise, assumes the existence of an *animating principle*, by which every organism is moulded into shape, out of materials furnished by the parent, and which, pervading the substance, regulates the various functions of its corporeal residence. But, at a subsequent stage of his inquiries, in assigning the blood as the special seat of this principle, he advances another supposition totally at variance with his previous hypothesis; namely, that as, during the development of the chick in ovo, the blood is formed and is moved, before any vessel, or any organ of motion exists, so in it and from it originate, not only motion and pulsation, but animal temperature, the vital spirit, and *even the principle of life itself.* So completely biassed were the views of this illustrious man, by his exaggerated notions respecting the nature and properties of the blood! Nor are many writers, in our own days, free from such vague notions. One who endeavours to introduce a new vital philosophy talks about the brain cells being the highest *parasites* (*!*) which live upon the *life of the blood.* And very many persons speak of the blood as distributing "life" to the tissues, as if life were something that could be caused to circulate in solution in a fluid, and be separated from it, and absorbed by this or that tissue!

The celebrated John Hunter, who does not appear to have been acquainted with the views expressed by Harvey, revived

a somewhat similar hypothesis; and it is curious that the same fact should have so attracted the attention of both as to have given the first impulse to their speculations. This fact was, that a prolific egg will remain sweet in a warm atmosphere, while an unfecundated one will putrefy. The views of Hunter were received with very general favour by English physiologists.

Hunter ascribes the phenomena of life to a *materia vitæ*, diffused throughout the solids and the fluids of the body. This *materia vitæ* he considers to be "similar to the materials of the brain;" he distinguishes it from the brain by the title "*materia vitæ diffusa*," while he calls that organ "*materia vitæ coacervata*," and supposes that it communicates with the former through the nerves, the *chordæ internunciæ*. And Mr. Abernethy, in commenting upon these views, explains Mr. Hunter's *materia vitæ* to be a subtile substance, of a quickly and powerfully mobile nature, which is superadded to organization and pervades organized bodies; and this he regards as, at least, of a nature similar to electricity. Such doctrines need no comment.

Müller advocated the presence of an "*organic force*," resident in the whole organism, on which the existence of each part was supposed to depend, and which had the property of generating from organic matters the individual organs necessary to the whole. "This rational creative force is exerted in every animal strictly in accordance with what the nature of each requires; it exists already in the germ, and *creates* in it the essential parts of the future animal."

An hypothesis, not dissimilar to the last mentioned, was advocated by Dr. Prout, and he supposed that a certain *organic agent* (or agents) exists, the intimate nature of which is unknown, but to which very extraordinary powers are ascribed. It is superior to those agents whose operations we witness in the inorganic world; it possesses the power of controlling and directing the operations of those inferior agents. "If," says Dr. Prout, "the existence of one such organic agent be admitted, the admission of the existence of others can scarcely be withheld; *for the existence of one only is quite inadequate to explain the infinite diversity among plants and animals.*" "In all cases it must be considered an ultimate principle, endowed by the Creator with a faculty little short of intelligence, by means of which

it is enabled to construct such a mechanism from natural elements and by the aid of natural agencies, as to render it capable of taking further advantage of their properties, and of making them subservient to its use."

The hypotheses of Aristotle, Müller, and Prout, and the earlier of those proposed by Harvey, seem all alike; they assume that organization and life are directed and controlled by an Entity, or Power, "endowed with a faculty little short of intelligence," the ψυχη of Aristotle, the animating principle of Harvey, the organic force of Müller, and the organic agent of Prout. What the mechanism may be by which this entity acts, they do not determine; but it is evidently such as bears no analogy to any known natural agency. Its existence is independent of the organism, for it has directed both the organising process and the living actions of the being. Whence then is it derived? According to Müller, from the parent, for it exists in the germ,—it derives its powers from the same source, and its pedigree may therefere be traced to the first created individual of each species of animal or plant. Are we to conclude, then, that organic agents generate organic agents, and transmit their powers to their offspring? Or must we assume, that, for each newly generated animal or plant, a special organic agent is deputed "to control and direct" its organization, development, and growth?

But many phenomena of the utmost importance to living beings, as already shown, are in their nature physical and chemical, and the laws under which they occur are well understood. The changes effected in the air and in the blood by respiration, the phenomena of absorption, and, in some degree, those of secretion, are the results of purely physical processes. It is in the highest degree probable that many of the actions of the nervous system are due to physical changes in the two kinds of nervous matter, substances of complex constitution and high equivalent number, and therefore prone to change. The generation of heat is due to the same chemical phenomenon as will give rise to it in the inorganic world; and electricity is also similarly developed within the body. How entirely dependent on physical changes are the senses of vision and hearing, and how completely are their organs adapted to the laws of light and sound.

The resistance which living animals introduced into the stomach are capable of offering to its solvent powers, and the digestion of the walls of the stomach by its own gastric juice, after sudden and violent death, seemed to denote that the dead animal or dead stomach had lost a something which previously protected them against the influence of the gastric fluid. This something, according to Hunter, was the *materia vitæ*, according to Prout, the organic agent. But such a result as this can be explained in a very simple way according to the view of structure given in Chapter I. In the texture still connected with the body of a living animal, and for a certain time after its removal, currents of fluid are continually passing through every part of the formed matter or tissue, to and from the masses of germinal or living matter, which are regularly distributed through it. This slow circulation of fluid derived from the blood, continues in a definite direction as long as the germinal matter remains alive; and while it continues the tissue cannot be permeated by another fluid. When the germinal matter dies, however, all these currents cease, and any fluid with solvent properties in which the tissue may be immersed, as the gastric juice, soon permeates it and dissolves it. So that the tissue is not prevented from being dissolved, by the influence of any vital force or power, but simply by the presence of fluids which permeate it in definite directions while it still lives; the flow of these fluids ceasing as soon as the living matter of the tissues dies. Thus it is that a living tissue resists the action of the gastric juice, and a dead tissue, or more correctly speaking a tissue, the germinal matter of which has ceased to live, and to and from which currents have in consequence ceased to flow, is soon dissolved by it. The process of digestion itself is probably only chemical solution.

So much for the dependence of life and organization on a controlling and directing *entity*. John Hunter rejected this doctrine entirely, but, as has been stated, went so far as to assume the presence of a peculiar *material of life*, which he maintained pervaded the organism and gave vital properties to solids and fluids. If, however, such a constituent existed in the body, it ought to be demonstrable by chemical or other means. Mr. Abernethy's doctrine that this *materia vitæ* was electricity or something akin to it is opposed to obvious facts. Electricity

requires for its development the reciprocal action of different kinds of matter, and it is abundantly evolved in various changes taking place in living beings as the necessary result of the action of well known chemical laws. If, therefore, organization and vital operations were due to electricity, this agent would at once be *formed by, and govern and direct* the formation of, each organism.

On the whole, we may conclude, then, that the theory which attributes the phenomena occurring in living organisms to the action of physical and chemical forces alone, rests upon no secure foundation, and is indeed controverted by important facts, and that the opposite doctrine, which supposes the existence of a *materia vitæ*, or of a *subtile* organic *agent*, possessing powers little short of reason, is equally untenable.

We have seen that the phenomena usually termed vital really comprise two distinct classes of actions—actions purely *physical and chemical*, and actions purely *vital*.

The truly vital actions which have been alluded to can only be accounted for by attributing them to the influence of some peculiar power totally distinct in its nature from any form of ordinary force. This is not a power which exists as it were in a concentrated state in the germ, and gradually expends itself as the tissues are evolved, or as the development of the race proceeds, but it is a power which is temporarily associated with, and influences for a brief period of time, every particle of matter which becomes living. It is a power which may be transmitted infinitely through the infinite multiplication of living matter without any increase or diminution in its intensity. As soon as tissue or any of the peculiar compounds result from the changes occurring in this living matter, its wonderful vital powers have ceased for ever.

Of the so-called vital stimuli. Many suppose that organized bodies being acted upon by certain vital stimuli develop vital actions. Thus heat is supposed to be the vital stimulus which *excites* the changes resulting in the development of the chick, light is supposed to excite or stimulate certain changes going on in the vegetable organism, nay, lifeless inorganic matter is regarded as an excitant to increased vital action in certain cases. A particle of sand falling upon the conjunctiva is followed by increased action as shown by the more rapid growth

of cells, and increased vascularity. It is said the particle of sand has *excited* these changes. It is an *irritant*. But the heat, light, and particle of inorganic matter are probably all perfectly passive. They have not been instrumental in actively *exciting* changes, but the conditions under which life was carried on before, have been altered, and the alteration is really due to changes not in the living matter, but in the formed lifeless matter by which it is surrounded. In consequence it permits pabulum to flow towards the living matter *more readily* than before. The living matter is not *excited* to live faster, but in consequence of more pabulum having access to it, more matter becomes living within the same period of time. The influence of the *excitant* is therefore of a passive character. It does not excite dormant energies or evoke vital actions, but by it some of the restrictions under which the matter lived previously are removed.

It is remarkable in these days, when the explanation of phenomena by hypothetical agencies, forces, or powers is assailed on all hands, that even some of those observers who have been specially distinguished for their opposition to any doctrine which admits the influence of vital as distinct from physical force, should pertinaciously insist, and without attempting to explain by what mysterious means, that a living cell can exert a modifying influence upon the action of cells around it. A cell undergoing increased action is supposed to excite increased action in those cells in its immediate neighbourhood. For example, Professor Virchow asserts that cells may be *incited* by a *stimulus* directly applied to them to take up an increased quantity of material. He maintains that every vital action presupposes an excitation or irritation. The illustration he gives for the purpose of explaining what he means by *irritation* will perhaps enable the reader to form a clearer notion of the views entertained upon these matters in the present day than a long exposition of the doctrines themselves. "Suppose three people were sitting quietly on a bench, and suddenly a stone came and injured one of them, the *others* would be *excited*, not only by the sudden appearance of the stone, but also by the injury done to their companion, to whose help they would feel bound to hasten. Here the stone would be the *irritant*, the injury the *irritament*, the help an expression of the *irritation* called forth in the bystanders." So that not only have the

uninjured cells a power of sympathising with their less fortunate companions, but they manifest a desire to hasten to afford them active assistance in their difficulty!

Such a doctrine is perhaps not more untenable or more unsupported by evidence than that which gives to insoluble inanimate matter the power of *exciting increased action* in living things. In every one of the cases in which this increased action occurs, it may be explained by the increased facility of access of pabulum to the living matter which is brought about by the so-called irritant or excitant. When a particle of sand, falling upon the conjunctiva, causes the removal of a portion of the outer layers of cells which in the normal state form a smooth membranous investment of uniform thickness, the thickness of this tissue protecting the vessels is diminished at the seat of injury, and as a matter of course a larger quantity of nutrient matter will permeate the thin layer which remains in a given time.

Again it must be remarked that even in the present day many observers admit the existence of some sort of power or force or agency which *directs or controls* the operation of the various actions going on in different parts of an organism, and is supposed to exert its influence through cell walls and other tissues, and to be capable of governing and regulating if not determining, the changes which take place in matter situated at some distance, and in the formation of which it has taken no part. Dr. Carpenter speaks of a power manifesting itself in organisms, which, according to him, exerts upon the cells and other structures, as well as upon the forces concerned in their production, a control which may be compared with that exercised by the "superintendent builder who is charged with the working out of the design of the architect." The germ supplies the "directive agency" and a distinction is made between *directive agency* and *constructive force*, which last is maintained to be but another mode of *heat*. Dr. Carpenter also speaks of "germinal capacity," but this, according to him, is a *condition* which, although transmitted from one organism to another, has its parallel in the inorganic world, in the fundamental difference in properties which constitute the difference between one substance, whether elementary or compound, and another! Now those phenomena which are ascribed by Dr. Carpenter to what is termed Germinal Capacity and Directive Agency, are

not peculiar to the germ, for there is not a living cell in any organism at any period of life in which such phenomena are not manifested in some degree. Moreover, long before any tissue is produced, a mass of living matter may be removed from an organism and carried far away from the influence of "directive agency," and may nevertheless give rise to tissues like those of the organism from which it was derived. Is the directive agency capable of being divided and subdivided, each subdivision having an influence equal to that of the whole? If so it can hardly be compared to the control exercised by the superintendent builder.

Mr. G. H. Lewes defines life as "a series of definite and successive changes, both of structure and composition, which take place within an individual without destroying its identity." It is doubtful if a *series* of changes is necessary to life; all we know is that lifeless matter passes into living matter and lives. Living matter exhibits no structure whatever, so that life may certainly exist without involving changes of structure. The definition seems to apply to the life of man and the higher animals rather than to living things generally. There are many masses of living matter which cannot be regarded as individuals. A white blood corpuscle or a pus-corpuscle is alive but it exhibits no structure and we know nothing of its composition while it lives. It cannot be regarded as an individual unless an individual may consist of millions of individuals, and many of these individuals differ from one another in very many essential points. Moreover, when a mass of living matter takes pabulum, increases in size and divides into numerous masses, what becomes of its identity? Such words as "individual" and "identity" would destroy the value of any definition.

Mr. Herbert Spencer proposes to define life as "The definite combination of heterogeneous changes, both simultaneous and successive, in correspondence with external co-existences and sequences." While this definition does not exclude lifeless machines it is doubtful if it would include many things which possess life although apparently quiescent. This writer, however, admits "the *tendency* to assume the specific form, inherent in all parts of the organism," which is peculiar to living things. He does not, however, attempt to explain the nature of the *tendency*, or why living matter alone exhibits it. What causes

the tendency? We know that the particles do actually arrange themselves in a very peculiar and special manner which cannot be imitated, and we want to know why they do so. Is it unreasonable to suppose that they take up their peculiar and constrained position in consequence of being influenced by a very peculiar force or power? It is difficult to help calling for an hypothesis to account for the tendency to assume specific form, which is admitted.

It has often been suggested that the movements of living beings are due to physical changes, but it must be borne in mind that different classes of movements are observed in connection with living beings. Under the head of *contractility* have been described several phenomena differing in their essential nature. For instance, the contractility of muscle, the vibration of cilia, and the oscillations of the spermatozoa, are different in their nature from the movements observed in the white blood corpuscle, pus and mucus corpuscle, and in many of the lowest and most simple organisms, such as the amœba, the foraminifera, &c. These and other movements will be considered in Chapter III; but with reference to the latter class of movement it may be at once remarked that they cannot be accounted for by physics, nor are they to be explained by any chemical changes occurring in the matter itself. They have been referred to osmosis, and to diffusion, but no such movements as these occur when conditions favourable to diffusion exist, while, even if they had been shown to depend upon these processes, we should still have to learn how the substance concerned in these movements was produced. The motion does not at all resemble any other kind of motion whatever. The moving power seems to reside in the particles themselves, and if such a moving mass be divided into several small portions, each portion will exhibit movements, while any very sudden shock, as of electricity, will at once destroy the capacity for movement, and at the same time cause all those phenomena which we regard as evidence of life to cease for ever. It has been assumed that these movements are peculiar to certain cells or bodies, and they have been termed "amœbiform cells" in consequence, but it will be shown that such movements occur in every form of living matter. They are peculiar to living matter, but not to any special organisms.

It is to be regretted that many who have recently written upon the subject of *life* have not expressed themselves clearly. Not unfrequently assertions are met with which are incompatible with one another, and even in the writings of the best modern thinkers there is much that is obscure and indefinite. Almost every writer seems to avoid stating in what points the simplest living things resemble, and in what they differ from, inorganic matter, and instead of discussing in the first place the nature and causes of the phenomena occurring in a mass of the simplest living matter, and then proceeding to the consideration of those observed in more complex organisms, the latter are almost exclusively referred to. Very different classes of phenomena are often included under the same head, and futile attempts made to account for opposite and antagonistic actions by the same hypothesis.

Although we are quite unable to say what sort of force vital power is, to isolate it, to examine it, or to give any satisfactory account of the exact manner in which it exerts its peculiar influence upon inanimate matter, we seem compelled to admit the existence of such a power, because the facts observed cannot be explained without such an admission. Every attempt hitherto made to account for the various phenomena which occur in living beings by physical actions alone has signally failed, and although some physiologists still hold to this view, they are compelled to ignore those phenomena which they cannot explain, and to discuss only those which occur *after* the peculiar (vital) actions have ceased to manifest themselves. They in fact describe as *vital acts* the destruction of peculiar substances which subtances resulted from the death of living matter, which occurred perhaps a long time before.

Strange as it may seem, it has been argued that as these unquestionably physical changes were formerly considered to be due to vital forces, physical forces only are concerned in vital phenomena. If those who hold such opinions would follow out the changes which occur throughout the life of the simplest organism, or even single cell, they would probably soon be convinced that something more than physical agency was required to account for the results observed.

It is unsatisfactory to many minds to be thus compelled to

admit the action of a force or power of the nature of which nothing is yet known, but it is better to do so than to pretend to be able to give a satisfactory explanation of phenomena which science in its present state is incompetent to account for.

Nevertheless an attempt has been made here, to assign to the word *vital* a definite meaning, and to distinguish *vital* from *physical* actions. It has been shown that besides the actions which may be explained upon the same principle as actions taking place in inanimate matter there are changes in every living being, and in every cell, which cannot be so explained or accounted for, which are peculiar to matter derived from living beings. Whatever the real nature of these changes may be, they cannot result from the action of any ordinary force, nor do they obey the same laws. The seat of these peculiar actions has been pointed out, and has been distinguished from the seat of the physical and chemical changes.

It will be remarked that the view of the vital processes advocated in these pages differs from others in the very essential point, that the assumed vital power is supposed to influence only particles of matter with which it is associated, and its association with matter is but temporary. The power bears neither a qualitative, nor as far as can be at present proved, a quantitative relation to the matter. It cannot act upon matter at a distance, nor upon the same particles for any length of time. The particles are influenced by it, but soon pass from its control. If their place is not soon succeeded by new particles, vital action must cease, but as long as new particles come into contact with those which live already, the action is transmitted, and so on for ever (not simply transferred from particle to particle so that one gains what another has lost). The direction and control exerted, are exerted upon particle after particle. The various particles are not placed in this or that place by a controlling power, ordering and influencing all, but each particle for the time being seems to direct and control itself, and its power is transmitted to new particles without loss or diminution in intensity, and sometimes with actual increase.

Certain physical conditions interfere with the manifestation of this power. The action of air, and various external circumstances, cause death. In fact it would seem that inanimate matter to become living, must come into contact with that which

lives, only in exceedingly minute portions at a time. If much lifeless matter comes into contact with living matter, the latter dies. Death is simply the cessation of the vital changes, and is due alone to the action of physical conditions. Physical forces invariably cause death, but they cannot give rise to life. Ordinary force and life seem to be opposed.

OF THE DIVERSITY OF FORMS OF LIVING BEINGS.

How shall we explain the strange process of organization, in the production of that infinite diversity of forms, that "insatiable variety of Nature," which is so conspicuous in the vegetable and animal kingdoms? The view that has been most generally entertained is, that the living matter of each species of animal or vegetable was created to propagate after a certain fashion, and after that only; the living matter of which these organisms consist in the early stages of development, must have the power of evolving the adult tissues of animal or plant of its own species only; the simple volvox develops, from its interior, matter which becomes volvoces; and the cell which forms the important part of the ovum of the elephant or the mouse, is able, by an inherent power of multiplication, to evolve the tissues and organs peculiar to each of those animals respectively.

The particular endowments of the organic matter, composing the various tribes of animals and plants, are transmitted from parent to offspring. But, as is well known, they admit of certain modifications under the influence of circumstances affecting the parents, as is proved both in the animal and vegetable kingdoms in the production of hybrids, and of forms differing in certain characters from either parent. "Two distinct species of the same genus of plants," says Dr. Lindley, "will often together produce an offspring intermediate in character between themselves, and capable of performing all its vital functions as perfectly as either parent, with the exception of its being unequal to perpetuating itself permanently by seed; should it not be absolutely sterile, it will become so after a few generations. It may, however, be rendered fertile by the application of the pollen of either of its parents; in which case its offspring assumes the character of the parent by which the pollen was supplied." The same thing precisely occurs among animals, and the mule, produced by the union of different species, is

incapable of breeding with another mule, although it may produce offspring with an animal of the same species as either of its parents.

Various facts show that physical agencies exert an important influence in modifying organic development. The most potent cause of these changes has been climate; but particular customs and usages, connected with the uncivilized state, have not been without their influence. Climate also produces considerable modifications in the size and other characters of the lower animals. The very striking alterations in character which are known to result from the influence of such external conditions has led many observers to suspect that still more important modifications may really be due to these causes alone, and that possibly two or more different species may have been produced by the action of dissimilar physical conditions upon the descendants of different members of the same original stock. It is true that the mind attempts in vain to realize the direct immediate creation of a living being out of inorganic matter, and it is therefore not to be wondered at that from time to time strong opposition to the old view, regarding the origin by separate special creations, of all the countless beings which surround us, should have arisen, or that attempts should have been made to substitute for it some theory which should account satisfactorily for the phenomena, without the necessity of accepting a dictum, or adopting an assumption which cannot be proved. But it is remarkable that some of the strongest opponents of the old account of the creation, experience no difficulty in accepting the doctrine of the spontaneous or fortuitous origin of organic particles, and their aggregation to form living organisms. No one attempts to explain how the atoms composing the first living particle, brought themselves together, any more than the nature of the forces associated with the inorganic atoms prior to their concourse, or the condition of the matter at a still earlier period than this, to say nothing of the origin of the matter itself.

Of late years the idea has been gaining ground that all the different plants and animals which exist, and which have existed from the beginning, have resulted entirely from the constantly modifying influence of continually altering external circumstances upon what was originally a very simple form. And

although the facts of the case compel the admission of inherent forces, acting as it were, from within living beings, the internal changes themselves have been attributed to the influence of pre-existing external conditions.

The origin of a single, growing, multiplying mass of formless, structureless, organic matter being admitted, it is said that countless modifications in structure and function of the masses resulting from it, and their descendants, are easily explained by the modifying influence of the different external conditions to which these must be subjected as the numbers increased, and necessarily became removed from the spot where the first concourse of inorganic particles, with its mysterious result, occurred.

Of all the views ever advanced in this direction, those of Mr. Darwin, "On the Origin of Species, by the process of Natural Selection," published in 1859, have received the warmest support, and although we cannot attempt to give more than a very rough outline of this view, the hypothesis is so full of interest, and is so fertile of investigation, that we shall draw attention to it in few words, and refer the reader for further information to the work itself.

The offspring of living beings, it has been truly observed, exhibit a tendency to inherit the characters of those from which they sprung. This is termed *atavism.* But there is also a tendency in the offspring to vary in certain particulars from the original stock, and an alteration having occurred is transmitted to the descendants. Now if it so happens that any of these modifications from the primitive type give advantages to their possessors over those which have them not, it follows that in the struggle for existence individuals of a species which vary in a way advantageous to themselves, possessing perhaps greater facilities for obtaining food, or greater power of resisting external destructive agencies, will survive and multiply, while their less fortunate fellows will gradually die out. In this way the former will be "naturally selected" from the latter, and by the strong tendency to inheritance, any variety thus selected will propagate its newly-acquired form. The tendency to the production of new characters, and the tendency to transmit these to the descendants, working through infinite time, must, it is argued, produce great differences in the character of the various

organisms descended from the same primary stock. The modifying influences of external circumstances, climate, food, temperature, acting through infinite time, and varying remarkably in places remote from one another, and in the same places, in successive epochs, will undoubtedly account for changes in character. Peculiarities thus arising, it is obvious may be further developed or diminished, according as the conditions by which they were induced persist, or become replaced by new ones. Although Mr. Darwin himself does not attempt to explain how many of these peculiarities arose, some seem to have regarded them as the result of accident occurring at a very early period of embryonic life, while many, who do not seem to admit that the supposed original simple living form, or forms, were endowed with any internal powers whatever at the time of their origin, attribute them to the influence of external circumstances alone.

By selective breeding, in certain cases, for many generations, very different forms undoubtedly result, so different, indeed, that a superficial observer might consider them at least as distinct as many creatures, admitted upon all hands, to be truly distinct species; and if the same modifying causes continued, it is difficult to conceive to what extent the modifications might proceed. It is urged there is no limit to the continuance and augmentation of changes thus induced. But all the instances hitherto adduced differ from true species in one very important particular. Members of different species seldom breed with one another, and in the few instances in which this does take place, the resulting mules or hybrids, if they are not absolutely barren, never breed with mules of the same kind, so that there is this most important fact opposed to the application of conclusions arrived at from observations upon varieties of one or more domestic species to the production of the various and undoubtedly distinct species of animals and plants now existing. The offspring of mere varieties is fertile, and they breed one with another, and there seems no limit to the varieties that may be produced in certain cases, but for this reason they must be considered varieties and not species.

It must not, however, be forgotten that the tendency to vary under altered conditions is not manifested in very many species of existing animals. The slightest alteration in external

conditions, at once destroys certain animals and plants. They do not live long enough to be modified by physical agencies. The capacity for existence, under a variety of different conditions, and tendency to gradual structural alteration, in consequence, seems indeed to be limited to comparatively few of the existing species of animals and plants. It would appear as if the life of the great majority of living beings was almost *dependent* upon the persistence of the particular external circumstances under which they happen to live. Moreover, the degree of change which actually occurs in different animals, which are capable of being domesticated, is very great. A familiar and very striking example occurs in the case of cats and dogs. How few the varieties of the former, and how comparatively slight the variation which does occur as compared with the latter. The organization of the cat is, as it were, much less plastic than that of the dog.

Looking at the facts broadly and generally, there undoubtedly seems much in favour of Mr. Darwin's view, but when we come to consider the structural changes which must occur in a single organ of one of the higher animals, it is more difficult to accept his conclusion. Changes occurring in each stage of development of a single organ seem continuously associated with others which occurred during those of a prior stage, and the changes affecting every part of one organism appear to be due to some general cause acting upon the whole from the very first. Creatures, undoubtedly very closely allied to one another, differ from each other, not in one or two, but in a vast number of characters. Although they may be much alike in form, and closely allied zoologically, they exhibit *physiological* differences of the most remarkable kind; and although there is some general accordance in the life history of distinct species, the differences of detail are far more striking and remarkable than, and quite as difficult to account for as, the general resemblances which have attracted notice.

In that temporary state in which all matter exists before it assumes the structure and composition peculiar to the different tissues of different living beings, no differences can be detected by any means yet known. The living matter of an adult tissue could not be distinguished from that of an embryo. Nor could the living matter of the highest brain cell of man be distin-

guished from that concerned in the production of the lowest living structure. And yet how different are the results of the life of the two? This difference would be more readily accounted for upon the hypothesis of the existence of some marvellous original difference in the *power* of the different kinds of living matter, than by the action of the different external circumstances under which descendants from one and the same stock have passed, or upon the hypothesis of the inherent tendency to vary. Can we accept the conclusion, that there was no well-defined difference at an early period of the world's history between the living forms then inhabiting the earth, until we have studied in detail the structure, mode of development, and complete life history of two existing species of simple organization, which are closely allied to one another? As yet we have no history of the life of any living thing which at all approaches completeness. It should be stated that, according to the theory, as accepted by many, something which amounts to a special creation is admitted to have occurred in the case of the first living molecule. The argument is supposed to commence from this point.

The anatomical differences between corresponding tissues of closely allied species are often so distinct that the anatomist familiar with them could distinguish one from the other. For example, it would be difficult to state in few words the differences between the unstriped muscular fibres of the bladder of the hyla, of the common frog, and of the newt, and yet there is a recognizable difference, and corresponding differences can be demonstrated in other textures, if a comparison be carefully instituted. So also with regard to the chemical composition of the corresponding solid matters, fluids, secretions, &c., of closely allied animals, remarkable differences are observed as may be demonstrated by a careful examination of the blood, bile, or urine, for example. Such differences affecting the minute structure, and chemical composition, of every part of the organism of creatures closely allied, are strong arguments in favour of the doctrine of the independent origin of distinct species; for it is scarcely reasonable to assume that any divergence in a few particulars, from the general characters of the common original stock, should be accompanied by, or should necessarily involve, a change in *all* these points, unless such

differences can be demonstrated to have occurred in the varieties of existing species; but this is a subject which has not yet been touched upon by Mr. Darwin or by those who have embraced his views. Animals may differ in many characteristics but still retain the most striking resemblance in all essential biological characters, or they may resemble one another in external form and general characters but differ most materially in internal structure. If a careful comparison should be made of everything in connection with the formation of structures throughout the life of closely allied but distinct species and between the most different varieties of the same species, it is probable that such essential points of difference in the one case, and agreement in the other, would be demonstrated as would suffice to convince the warmest advocate of Mr. Darwin's views that more minute investigation was required before his doctrine, as applied to the origin of all species, could be admitted to rest upon a satisfactory basis.

OF PLANTS AND ANIMALS AND OF THE FUNCTIONS.

It is impossible to define precisely a boundary between the vegetable and animal kingdoms, and any attempt to lay down characters which shall distinguish plants from animals in every case must fail. The lowest animals are said to exhibit so much of the plant nature that naturalists are as yet undecided as to the true location of some species. The common sponge, for instance, a short time since was claimed for each kingdom, but there can now be no doubt of its animal nature. The important phenomena of plant and animal life are, in fact, the same in their essential nature. Still it will be advantageous to recount briefly some of the most important general characters in which the fully developed animal differs from, or agrees with the fully developed plant.

The first step in the nutritive functions of both plants and animals, is to form a fluid, which contains all the elements necessary to nourish the various textures, and to supply materials for the secretions. This fluid is, in plants, *the sap;* in animals, *the blood.*

In both classes of beings a process of *absorption* precedes the full development of the nutritive fluid: it is by this means that

material is obtained for its formation. Within the plant or animal it becomes more completely elaborated.

In plants, the absorption takes place by the spongioles of the roots. A fluid, already prepared in the soil,—water, holding in solution carbonic acid and various mineral substances,—passes through them into the vegetable organism. In animals the food experiences much change, and a more or less elaborate process of *digestion* takes place, before a fluid is formed, capable, when absorbed, of furnishing the materials of the blood.

Plants, fixed by their roots in the soil, imbibe from it their nutriment. Animals, obtaining food from various sources, introduce it into a digestive cavity, where it is prepared for absorption.

The presence of a digestive organ, or stomach, is characteristic of animals. The only instances in which a similar organ may be supposed to exist in the vegetable kingdom, are to be found in those remarkable modifications of leaves, called pitchers (*ascidia*) in *Nepenthes*, *Sarracenia*, and *Dischidia*. In the last two plants, these organs certainly serve to retain and dissolve the bodies of insects in the fluid which partially fills them: in *Sarracenia*, according to Mr. Burnett, the fluid contained in the pitchers is very attractive to insects, which, having reached its surface, are prevented from returning by the direction of the long bristles that line the cavity. The dissolved food is then absorbed into the plant.

On the other hand, the animal kingdom affords some exceptions to the presence of a stomach. In such animals, the absorption of nutrient fluid takes place by a general surface. Many of the infusoria are destitute of a stomach. A parasite of the human body, the *Acephalocyst*, also derives its nutriment by imbibition through its walls. A familiar example is the *Acephalocystis endogena*, or pill-box hydatid of Hunter. It consists of a globular bag, closed at all points, containing a limpid fluid, capable of growth, developing upon the inner surface of the sac little organisms, also nourished by absorption, the echinococci, which are the early stage of development of what was onee supposed a distinet species, the tapeworm.

Some differenee may be noticed as regards the nature of the food in animals and plants. The former derive their nutriment entirely from the organized world, unless, indeed, we suppose

that the nitrogen absorbed in respiration contributes to their sustenance. Plants appropriate inorganic elementary matters for food, as carbon, carbonic acid, ammonia, &c. "Inorganic matter," says Liebig, "affords food to plants; and they, on the other hand, yield the means of subsistence to animals. The conditions necessary for animal and vegetable nutrition are essentially different. An animal requires for its development, and for the sustenance of its vital functions, a certain class of substances which can only be generated by organic beings possessed of life. Although many animals are entirely carnivorous, yet their primary nutriment must be derived from plants; for the animals upon which they subsist receive their nourishment from vegetable matter. But plants find new nutritive material only in inorganic substances. Hence one great end of vegetable life is to generate matter adapted for the nutrition of animals out of inorganic substances which are not fitted for this purpose."

The nutrient fluid, however formed, is distributed throughout the textures of the plant, or animal, by vital or physical forces, or by the junction of both; and the function, by which this is effected, is called *Circulation*. In plants, this function is very simple, and is performed without the agency of a propelling organ, circulating through capillary vessels which exist in every part of the tissues of the plant. In some plants, the fluid is found to circulate, or rotate, within the interior of cells, as in *Chara* and *Vallisneria*, the fluid of one cell not communicating with that of the adjacent ones; or to pass up from the spongioles in an ascending current, and to descend in another set of vessels. In the greatest number of animals, a propelling organ, a *heart*, is the main instrument in the distribution of the blood. In animals, then, there is a true circulation; the fluid setting out from, and returning to, the same place. In many simple animals and plants, however, there is no circulation at all in special vessels, but the tissues are nourished by imbibing the elements of nutrition from the medium in which they are immersed.

The presence of atmospheric air is necessary to the existence of all organized beings. The air both passes by endosmose into their nutrient fluids, and receives from them certain deleterious gases developed in their interior. The function, by which the

fluids are thus aërated, is called *respiration.* In plants, the introduction of atmospheric air conveys nutriment to the organism; carbonic acid and ammonia are thus introduced; the former is decomposed, its carbon is assimilated, and its oxygen is exchanged for a fresh supply of atmospheric air. As the agent in the decomposition of the carbonic acid is light, it is evident that the generation and the evolution of oxygen can take place only in the day-time. Consequently, during the night, the carbonic acid, with which the fluids of the plant abound, ceases to be decomposed, and is exhaled by its leaves. Hence, plants exhale oxygen in the day-time, and carbonic acid at night.

In animals, carbonic acid accumulates in the blood during its circulation; and, when the atmosphere is brought to bear upon the capillary vessels containing the blood charged with this gas, a mixture takes place through the delicate walls of the vessels, the atmospheric air passing in, and carbonic acid, with nitrogen and oxygen, in certain proportions, escaping. Thus the evolution of carbonic acid, and the absorption of oxygen and nitrogen, are the characteristic features of respiration in animals. It is highly interesting to notice, how plants are thus subservient to the well-being of animals, in the respiratory function, as well as in preparing nutriment for them. By their respiration they serve to purify the air for animals; for, in absorbing the carbonic acid from the atmosphere, they are continually depriving it of an element which, if suffered to accumulate beyond certain bounds, would prove destructive to animal life.

From the fluids of animals and plants, certain materials are separated by a singular process, nearly allied in its mechanism to nutrition, and called the function of *secretion.* The secreted matters are various, and have very different ends: in some cases being destined for some ulterior purpose in the economy; in others, forming an excrement, the continuance of which in the organism would be prejudicial to it.

The function, which has for its object the propagation of the species, *generation*, presents many points of resemblance in plants and animals. In the former it is cryptogamic, or phanerogamic; in the latter, non-sexual or sexual. In the phanerogamic and sexual, the junction of two kinds of matter furnished by the parents is necessary to the development of fertile ova. In the

cryptogamic and non-sexual generation, the new individual is developed by a separation of particles from the body of the parent, by which the new formation is nourished until it has been so far matured as to be capable of an independent existence.

The functions, hitherto enumerated, may be called *organic*, as being common to all organized beings; but there are others which, as being peculiar to, and characteristic of, animals, may be appropriately designated *animal* functions.

The prominent characteristic of animals is the enjoyment of *volition* or *will*, which implies necessarily the possession of *consciousness*. Our knowledge of the share which consciousness and the will have in the production of certain phenomena of animal life, is derived from the experience which each person has of his own movements, and a comparison of them with the actions of inferior animals. We are conscious that, by a certain effort of the mind, we can excite our muscles to action; and when we see precisely similar acts performed by the lower creatures, with all the marks of a purpose, it is fair to infer that the same process takes place in them as in ourselves. Moreover, we learn by experience, that injury or disease of the nerves, which are distributed to our muscles, destroys the power of accomplishing a certain act, but does not affect the desire or the wish to perform it: and experiments tell us that the division of the nerves of a limb in a lower animal destroys its power over that member; while its ineffectual struggles to move the limb obviously indicate that the will itself is not affected by the bodily injury, though its powers are limited by it.

Again, certain external agents are capable of affecting the mind, through certain organs, thus giving rise to *sensations*. Light, sound, odour, the sapid qualities of bodies, their various mechanical properties, hardness, softness, &c., are respectively capable of producing corresponding affections of the mind, which experience leads us to associate with their exciting causes, and which may be agreeable, and produce *pleasure*, or the reverse, and give rise to *pain*.

In a similar way to that by which we learn that the will stimulates our muscles through the nerves, we can ascertain that the nerves are the channels through which our sensations also are excited. "Certain states of our bodily organs are

directly followed by certain states or affections of our mind; certain states or affections of our mind are directly followed by certain states of our bodily organs. The nerve of sight, for example, is affected in a certain manner; vision, which is an affection, or state of the mind, is its consequence. I will to move my hand; the hand obeys my will so rapidly, that the motion, though truly subsequent, seems almost to accompany my volition, rather than to follow it."*

And in all the inferior animals, possessed of like organs, there can be no doubt that sensations may be produced similar to those which arise in the human mind. In many of them, indeed, the sense of sight, hearing, or smell, seems much more acute than in man, and affords examples of a beautiful and providential provision for the peculiar sphere which the creatures are destined to occupy. The unerring precision of the beast or bird of prey in pouncing upon its victim—the accuracy with which the hound tracks by its scent the object of its pursuit—or the quickness with which most of our domestic animals detect sounds and judge of their direction, are familiar illustrations of the superiority of these senses in animals whose general organization is inferior to that of man.

There are few animals, however small and insignificant, in which we cannot recognize evidence of a controlling and directing will. But even in those few, in which voluntary movements are not distinctly to be discerned, the presence of a special system of organs, with which in the higher animals volition and sensation are associated, namely, a *nervous system*, serves as a characteristic distinction from plants.

A power of perception, and a power of volition, together constitute our simplest idea of *mind;* the one excited through certain corporeal organs, the other acting on the body. Throughout the greatest part of the animal creation mental power exists, ranging from this its lowest degree—a state of the blindest instinct, prompting the animal to search for food—to the docility, sagacity, and memory of the brute; and to its highest state, the reasoning powers of man.

The phenomena of mind, even in their simplest degree of development, are so distinct from anything which observation teaches us to be produced by material agency, that we are

* Dr. Brown. Philosophy of the Human Mind, p. 106.

bound to refer them to a cause different from that to which we refer many of the phenomena of living bodies. Although associated with the body by some unknown connecting link, the mind works quite independently of it; and, on the other hand, a large proportion of the bodily acts are independent of the mind. The immortal soul of man, *divinæ particula auræ*, is the seat of those thoughts and reasonings, hopes and fears, joys and sorrows, which, whether as springs of action or motions excited by passing events, must ever accompany him through the chequered scene in which he is destined to play his part during his earthly career.

Although the animals, inferior to man, exhibit many mental acts in common with him, they are devoid of all power of abstract reasoning. "Why is it," says Dr. Alison, "that the monkeys, who have been observed to assemble about the fires which savages have made in the forests, and been gratified by the warmth, have never been seen to gather sticks and rekindle them when expiring? Not, certainly, because they are incapable of understanding that the fire which warmed them formerly will do so again, but because they are incapable of abstracting and reflecting on that *quality* of wood, and that *relation* of wood to fires already existing, which must be comprehended, in order that the action of renewing the fire may be suggested by what is properly called an effort of reason."

Yet animals are guided by *instinct* to the performance of certain acts which have reference to a determinate end: they construct various mechanical contrivances, and adopt measures of prudent foresight to provide for a season of want and difficulty. None of these acts could be effected by man without antecedent reasoning, experience, or instruction. But animals do them without previous assistance; and the young and inexperienced are as expert as those which have frequently repeated them. "An animal separated immediately after its birth from all communication with its kind, will yet perform every act peculiar to its species in the same manner, and with the same precision, as if it had regularly copied their example, and been instructed by their society. The animal is guided and governed by this principle alone, by this all its powers are limited, and to this all its actions are to be ultimately referred. An animal can discover nothing new; it can lose nothing old. The beaver constructs

its habitation, the sparrow its nest, the bee its comb, neither better nor worse than they did five thousand years ago."

In plants there is no nervous system; there are no mental phenomena. The motions of plants correspond in some degree with those movements of animals in which neither consciousness nor will participate. Some of the movements undoubtedly result from physical changes produced directly in the part moved. Amongst the most interesting examples are those of the *Mimosa pudica*, the *Dionæa muscipula*, and the *Berberis*. But movements of another kind, as the movements in the interior of the cells of Vallisneria Tradescantia, &c., depend upon changes occurring in the living matter, the nature of which is not yet understood. These movements will be discussed in another place.

OF ANATOMICAL INVESTIGATION.

It is the province of physiology to investigate the manner in which the functions of living beings are carried out; and this investigation naturally involves the examination of their mechanism, of the chemical constitution, and of the properties of their component textures. The study of anatomy must always accompany that of physiology, on the principle that we must understand the construction of a machine before we can comprehend the way in which it works. The history of physiology shows that it made no advance until the progress of anatomical knowledge had unfolded the structure of the body. There is so much of obvious mechanical design in the intimate structure of the various textures and organs, that the discovery of that structure opens the most direct road to the determination of their uses. That kind of anatomy which investigates structure with a special view to function may be properly designated *Physiological Anatomy*.

In investigating the functions of the human body, the physiologist cannot do better than follow the instructions laid down by Haller in the preface to his invaluable work, "Elementa Physiologiæ Corporis Humani."

The first and most important step towards the attainment of physiological knowledge is, the study of the fabric of the human body. "Et primùm," says Haller, "cognoscenda est fabrica corporis humani, cujus penè infinitæ partes sunt. Qui

physiologiam ab anatome avellere studuerunt, ii certè mihi videntur, cum mathematicis posse comparari qui machinæ alicujus vires et functiones calculo exprimere suscipiunt, cujus neque rotas cognitas habent, neque tympana, neque mensuras, neque materiam."

A knowledge of human anatomy alone is, however, not sufficient to enable us to form accurate views of the functions of the various organs. Before an exact judgment can be formed of the functions of most parts of living bodies, Haller says, that the construction of the same part must be examined and compared in men, in various quadrupeds, in birds, in fishes, and even in insects. And, in proof of the value which attaches to this knowledge of *comparative anatomy*, he shews how, from that science, it may be determined that the liver is the organ which secretes bile; and that the bile found in the gall-bladder is not secreted by, but conveyed to, that organ; for no animal has a gall-bladder without a liver, although many have a liver without a gall-bladder; and, in every case where a gall-bladder is present, it has such a communication with the liver, that the bile secreted by the latter may be easily transferred to the former. "Vides adeò," he adds, "bilem hepate egere, in quo paretur, vesiculâ non egere, non ergo in vesiculâ nasci, ex hepate verò in vesiculam transire."

And Cuvier has happily compared the examination of the comparative anatomy of an organ, in its gradation from its simplest to its most complex state, to an experiment which consists in removing successive portions of the organ, with a view to determine its most essential and important part. In the animal series we see this experiment performed by the hand of nature, without those disturbances which mechanical violence must inevitably produce. We thus learn, from comparative anatomy, that the vestibule is the fundamental part of the organ of hearing; and that the other portions, the semicircular canals, the cochlea, the tympanum and its contents, are so many additions made successively to it, according as the increasing perceptive powers of the animals rendered a more delicate acoustic organ necessary. In a similar manner we learn, that one portion of the nervous system, in those animals in which it has a definite arrangement, is pre-eminently associated with the mind, and is connected with, and presides

over, the other parts. This organ, the brain, is always situate at the anterior or cephalic extremity of the animal, and with it are immediately connected the organs of the senses, the inlets to perception. We soon find that the brain exhibits a subdivision into distinct parts, and of the relative importance of these parts, and their connexion with the organs of sense, and with the intellectual functions, we derive the most important information from the study of comparative anatomy.

Haller further assigns the examination of the living animal as a valuable aid in physiological research. Many obscure points have been elucidated by experiments on living animals, and discoveries have been made which have greatly contributed to the progress of physiology. Very useful knowledge may be derived from observing the play of certain functions in living animals, or in man himself,—contrasting them in various individuals, and noting the effects of age, sex, and temperament, and ascertaining the influence which other conditions, natural or artificial, may exert upon them.

The investigation of disease, both during life and after death, is of great value in enabling us to appreciate the action of an organ in health. If, for example, as Haller remarks, a particular function be ascribed to a certain part, how can there be a more favourable opportunity of testing the accuracy of such a doctrine than by the examination of a body in which that part was affected with a disease, of which the previous history was known? If the function in question had been vitiated, or destroyed, it may be fairly presumed to have had its seat in the diseased organ. Nothing has contributed more largely to determine the functions of particular nerves, than exact histories of the symptoms during life, in cases in which they had been found, after death, in a diseased condition.

IMPORTANCE OF ANATOMY AND PHYSIOLOGY TO THE ADVANCE OF MEDICINE AND TO ITS STUDY.

A correct physiology must ever be the foundation of rational medicine. He who is ignorant of the proper construction of a watch, and of the nature of the materials of which it is made, could not find out in what part its actions were faulty, and would therefore be very unfit to be entrusted with repairing it. In medicine, the first step towards the cure of disease is to find

out what the disease is, and where it is situated (*diagnosis*). Without a knowledge of the offices which various parts fulfil in the animal economy, our search to determine what organ or function is deranged must be most vague and indefinite. *Pathology* is the physiology of disease; and it is obvious, that no pathological doctrines can command confidence, which are not founded upon accurate views of the natural functions. It is also certain that improvements in pathology must follow in the wake of an advancing physiology.

The practice of medicine and surgery abounds with examples illustrating the immense benefits which physiology has conferred upon the healing art. The great advance which has been made in the pathology of nervous diseases, is mainly owing to the discoveries of Bell, and more recently to the researches of Marshall Hall, Bernard, Brown-Séquard, and others, upon the functions of various nerves, and the general doctrines of nervous actions. We may instance the case of the facial nerve—the portio dura of the seventh pair. It was supposed formerly that this nerve was the seat of that painful disease, called *tic-douloureux*, and section of it has been performed for the relief of the patient. It is now known that this nerve could not be the seat of a very painful disease, for it is itself, in a very great degree, devoid of sensibility. It need hardly be added, that the operation is discarded.

The dangerous disease, to which many children have fallen victims, *laryngismus stridulus* or *crowing inspiration*, although admirably described by practical physicians, was never properly understood until the functions of the laryngeal nerves were clearly ascertained, and until it had been shown that spasmodic actions may be excited by irritation of a remote part, or through a stimulus reflected from the nervous centre. It is now known, that this disease has not its seat in the larynx, where those spasms occur which excite so much alarm for the fate of the little patient; but that it is an irritation of a distant part, which derives its nerves from the same region of the cerebro-spinal centres as does the larynx,—that the afferent nerves of that part convey the irritation to the centre, whence it is reflected by certain efferent nerves to the muscles of the larynx.

The important observations made of late years upon the

action of the sympathetic nerve upon the blood-vessels has already thrown great light upon the nature of numerous pathological changes, especially those complex phenomena which constitute what in the higher animals and man are termed congestion and inflammation. The recent researches upon the arrangement of, and course taken by, the nerves in the central organs conducted by Stilling, Lockhart Clarke, and others, are likely to lead to most important conclusions with reference to the actions of the brain and cord.

The accurate diagnosis of diseases of the heart rests entirely upon a correct knowledge of the physiology of that organ. This improvement in medicine may be said to date from the time of Harvey, for he was the first who clearly expounded the mechanism of the central organ of the circulation. But the application of auscultation to the exploration of the sounds developed in its action, and the correct interpretation of those sounds in health by the experiments and observations of the last few years, have almost completely removed whatever difficulties stood in the way of the detection of cardiac maladies.

We are not less indebted to the illustrious Englishman who discovered the circulation of the blood, for having paved the way to a rational treatment of aneurismal and wounded arteries by the modern operation of placing a ligature between the heart and the seat of the disease or injury. "The active mind of John Hunter," says Mr. Hodgson, "guided by a deep insight into the powers of the animal economy, substituted for a dangerous and unscientific operation, an improvement founded upon a knowledge of those laws which influence the circulating fluids and absorbent system; and few of his brilliant discoveries have contributed more essentially to the benefit of mankind."

THE USE OF THE MICROSCOPE.

For exploring the structure of the various textures, and the relation of the anatomical elements of the body to one another, the *Microscope* is necessary. The great improvements which modern opticians have accomplished, not only in the dioptric but also in the mechanical adjustments of this instrument, render it an invaluable adjuvant in physiological research. We shall have frequent occasion in the following pages to

refer to anatomical analyses, effected by the microscope, of the utmost value to the knowledge of function. New means of preparing tissues, and the use of powers magnifying upwards of 1,000 diameters, have enabled us to investigate details with a precision and to an extent which not long since was considered impossible. It may, however, be remarked, that, as the sources of fallacy are numerous even with the best instruments, more depends upon the observer himself, in this kind of investigation, than in almost any other.

The great impediment to deriving correct inferences from microscopical observations has arisen from the discordance, too apparent, in the narrations of different observers. This discordance has been the result of a twofold cause; namely, imperfection of the instruments, and the very unequal qualifications of different observers. The former cause is now almost completely removed; the latter must remain while men imperfectly appreciate their own abilities for particular pursuits.

Many observers have placed too much reliance upon minute and elaborate description of what they have seen, and have not been at the pains to give careful representations of the structure as it appeared to them. Others, although they have given drawings, have executed them very carelessly, and have omitted to draw them to a scale, so that they cannot be compared one with another, or with the drawings of other observers. Again, the system of one anatomist endeavouring to refute the statements of another by researches upon a different object, conducted upon a different principle, only serves to increase the confusion already existing, and to postpone to a more distant period the definite settlement of most important elementary principles. If anatomical observers would select the same organisms for study, and make their drawings as accurately as possible to a fixed scale, many of the questions upon which they are now at issue would soon be determined.

To make microscopical observation really beneficial to physiological science, it should be done by those who possess two requisites: an *eye*, which practice has rendered familiar with genuine appearances as contrasted with those produced by the various aberrations to which the rays of light are liable in their passage through highly refracting media, and which can quickly

distinguish the fallacious from the real form; and a *mind*, capable of detecting sources of fallacy, and of understanding the changes which manipulation, chemical re-agents, and other disturbing causes may produce in the arrangement of the elementary parts of various textures. To these we will add another requisite not more important for microscopical than for other inquiries; namely, a freedom from preconceived views or notions of particular forms of structure, and an absence of bias in favour of certain theories, or strained analogies. The history of science affords but too many instances of the baneful influence of the *idola specûs* upon the ablest minds; and it seems reasonable to expect that such creatures of the fancy would be especially prone to pervert both the bodily and the mental vision, in a kind of observation which is subject to so many causes of error as that conducted by the aid of the microscope.

Of late years, however, great improvements have been introduced in the mode of preparing specimens, and the chances of arriving at erroneous inferences very much diminished. The structures represented in the new plates, illustrating this work, have been prepared according to the same plan, and all the figures have been drawn to a scale, so that they may be compared one with the other. The methods of injecting with transparent Prussian blue fluid and staining the germinal matter of the tissues with carmine are described in detail in "How to work with the Microscope," but the student will find an outline of the plan at the end of the present chapter. This process of preparation is applicable to those specimens which require to be examined by the aid of very high magnifying powers, and it possesses this great advantage—that every tissue can be demonstrated in the same preparation.

During the last ten years we have had the advantage of the use of much higher magnifying powers than could have been obtained previously. The first $\frac{1}{25}$ ever made was the workmanship of Mr. Wenham, and was completed in June, 1856. In 1840, Messrs. Powell and Lealand succeeded in making a $\frac{1}{16}$, in 1860, a $\frac{1}{26}$, and in 1864 the same makers produced a $\frac{1}{50}$, the definition and penetrating power of all which glasses are exceedingly good. The first of these objectives magnifies about 1,500, and the last nearly 3,000 diameters linear.

PHYSICAL AND CHEMICAL INVESTIGATION.

Of late years our knowledge of physiology has been greatly advanced by physical investigation. The study of the processes of Diffusion, Osmose, and of the physical conditions of matter, has added much to our information regarding the nature of many changes occurring in the living organism. The invention of various ingenious instruments for ascertaining the force of the circulation has taught us many important principles which were unknown before. The further prosecution of investigations upon the electrical phenomena of living beings, a department in which great success has been already achieved by Matteucci, and more recently by Du Bois Reymond, promises most valuable generalizations. The still recent discoveries regarding the influence of the solar spectrum upon different substances have been already applied to the investigation of animal fluids, and important results have been obtained by Stokes, in connection with the changes occurring in the blood during the process of respiration.* Physical investigation has greatly advanced our knowledge of the wonderful phenomena of sight and hearing, and by the aid of various optical instruments we are now enabled to make a most minute examination during life of the tissues within the eye.

Haller perceived how necessary to the furtherance of physiology is a knowledge of *Organic Chemistry;* and we could adduce many instances to prove, that the attention which has of late years been paid to this subject, has been most fruitful in giving us an insight into the nature of many functions, which, without it, we could not have obtained.

In the living body the most delicate chemical processes are unceasingly going on, for the formation of new compounds and the alteration or destruction of old ones. It is evident that no progress can be made in the investigation of these invisible processes, unless we can arrive at an exact knowledge of the chemical composition of the various substances which are concerned in them.

Henceforward, in physiological research, physics, anatomy, and chemistry must go hand in hand. By the first the physical

* "On the Reduction and Oxidation of the Colouring-matter of the Blood." Proceedings of the Royal Society, No. 66, page 355, June, 1864.

phenomena, which play so important a part in the changes which take place in complex organisms, may be elucidated; by the second, the minute mechanism concerned in these phenomena is ascertained; by the third, the nature of the chemical analyses and syntheses taking place in the living organism are to be determined. Here is a wide field of research open for the employment of every kind of mind, and by devoting himself to one or other of these departments, every earnest student may contribute important aid to the advance of physiology, and thereby to the progress of medicine and surgery.

In the composition of the Introduction, the authors have to acknowledge valuable aid from the following works:—Haller, Elementa Physiologiæ Corporis Humani; Barclay on Life and Organization; Roberton on Life and Mind; Prichard on the Doctrine of a Vital Principle; Dr. Carpenter's article Life, and Dr. Alison's article Instinct, in the Cyclopædia of Anatomy and Physiology; L. Pasteur, papers in the Comptes Rendus, 1859—64; F. A. Pouchet, Hétérogénie; Joule, papers in the Phil. Trans.; Julius R. Mayer, Die Organische Bewegung; Tyndall, Heat as a Mode of Motion; Grove on the Correlation of the Physical Forces; Helmholtz, Erhaltsung der Kraft; Lectures at the Royal Institution; Carpenter on the Correlation of Physical and Vital Forces, Journal of Science, Nos. I. and II.; Graham's papers on Diffusion, Osmose, Crystalloids and Colloids, Phil. Trans. 1850—64; Darwin on the Origin of Species; Huxley, Lectures on the Origin of Species, and Elements of Comparative Anatomy; Carpenter, Principles of Physiology; Herbert Spencer's First Principles and his Principles of Biology; Beale, the Anatomy of the Tissues, the Microscope in Medicine, and papers in the Archives of Medicino and Microscopical Journal.

On the Preparation of the Tissues of Man and the higher Animals and Morbid Growths, for Microscopical Examination with high powers.

It has been thought desirable to describe briefly the general method which has been employed in preparing specimens for examination with the highest powers, in the hope that the student may be encouraged to pursue some of the inquiries entered upon in this work, and that many of the investigations may be extended still further.

In the first place, it is necessary to consider what circumstances interfere with the perfect demonstration of structure under the highest powers of the microscope, and how the disadvantageous operation of these might be prevented or diminished.

1. Of many tissues, sections sufficiently thin for high powers cannot be obtained by the processes usually adopted. In order to make the specimen thin enough, pressure must be employed, and in many instances very strong pressure is required. Even by very moderate pressure, tissues immersed in

water are destroyed completely, and experience has proved that the requisite amount of pressure can only be employed if the tissue be immersed in, and thoroughly impregnated with, a viscid medium, which is not only readily miscible with water in all proportions, but with such chemical reagents as may be required to act upon one or more constituents of the tissue for the purposes of demonstration.

2. As many structures are exceedingly delicate, and undergo change very soon after death, it is necessary that the medium in which they are examined should have the property of preventing softening and disintegration, and should act the part of a preservative fluid.

3. In order that tissues should be uniformly permeated with a fluid within a very short time after the death of the animal, it is necessary that the fluid should come quickly in contact with every part of the texture. This may be effected in two ways:—

a. By soaking very thin pieces in the fluid, or
b. By injecting the fluid into the vessels of the animal.

4. As different structures require fluids of different refractive power for their demonstration, the medium employed must be such that its refractive power can be increased or diminished, or that, for the medium fulfilling the former condition, another can be readily substituted which fulfils the latter requirements.

5. In investigations upon the changes which structure undergoes in the organism, it is necessary to distinguish between that part of the texture which is the oldest, and that which has just been produced—between matter in which active changes are going on, and matter which is in a passive state. It is only by fulfilling this requirement that the direction in which growth takes place, and the point where new matter is added, can be ascertained.

6. It is necessary, in many investigations, that the vessels should be positively distinguished from the other constituents of the tissue, and it is important that the process by which this is effected, should not interfere with the demonstration of all the tissues in the immediate vicinity of the vessels.

7. It is of the utmost importance the medium employed for demonstration should have the property of preserving the specimens, so that observers should be able to exhibit their preparations to others.

Glycerine and *syrup* fulfil the requirements mentioned in the foregoing paragraphs. Strong syrup may be made by dissolving, with the aid of heat, lump sugar in distilled water, in the proportion of about three pounds to a pint. It is necessary in many cases to employ the strongest glycerine. In this country we have had the advantage of the beautiful preparation called Price's glycerine, which is made of specific gravity 1240. It has been said that glycerine and strong syrup are not adapted for preserving soft tissues, because the tissues shrink and soft cells collapse in consequence of exosmose of their fluid contents. But I have many hundred specimens preserved in the strongest glycerine I could procure, and I should obtain advantages if glycerine could be made of still greater density. There would be no difficulty in impregnating even very soft tissues with it.

Tissues possess a considerable elastic property, and although they shrink

when immersed in a medium of considerable density, they gradually regain their original volume if *left in it for some time.* In practice, the specimen is first immersed in *weak* glycerine or syrup, and the density of the fluid is gradually increased. In this way, in the course of two or three days, the softest and most delicate tissues may be made to swell out almost to their original volume. They become more transparent, but no chemical alteration is produced, and the addition of water will at any time cause the specimen to assume its ordinary characters.

The hardest textures, like bone and teeth, may be thoroughly impregnated and preserved in strong glycerine, and the softest, like cerebral tissue, delicate nervous textures like the retina, or the nerve textures of the internal ear, may be permeated by the strongest glycerine, and when fully saturated with it, dissection may be carried to a degree of minuteness which I have found impossible in any other medium. Nor is the use of glycerine and syrup confined to the tissues of man and the higher animals. I have preparations from creatures of every class. The smallest animalcules, tissues of entozoa, polyps, star fishes, mollusks, insects, crustacea, various vegetable tissues, microscopic fungi, and algæ of the most minute and delicate structure, as well as the most delicate parts of higher vegetable tissues, may all be preserved in these viscid media ; so also may be preserved the slowest and most rapidly growing, the hardest and softest morbid growths, as well as embryonic structures at every period of development, even when in the softest state. I am, indeed, not acquainted with any animal or vegetable tissue which cannot with the greatest advantage be mounted thus. All that is required is, that the strength of the fluid should be increased very gradually until the whole tissue is thoroughly penetrated by the strongest that can be obtained. Glycerine has long been in use among microscopists, but my object is to show that it is universally applicable, that it or syrup may be made the basis of all solutions employed by the microscopical observer with the greatest advantage, that many points are to be demonstrated by the use of these solutions, which have hitherto escaped observation, and that there are reasons for believing that very much may yet be discovered by the use of these substances.

From these general remarks, I pass on to describe, more in detail, the particular method I have adopted during the last four years for minute investigations upon structures magnified by the highest powers yet employed. It will be necessary, in the first place, to give the composition of the different solutions which I find useful for general purposes.

1. *Weak common glycerine* of about the specific gravity 1050.

2. *The strongest Price's glycerine* that can be obtained.

3. *Syrup* made by dissolving, by the application of a gentle heat in a water-bath, 3lbs. of sugar in a pint of distilled water. A weaker solution can be prepared, as required, by mixing equal parts of syrup and water.

The two following solutions should be kept ready prepared. They will keep for a length of time. The first is required for rendering the vessels distinct. The last enables us to distinguish with certainty the *germinal* or *living* matter of every tissue from the formed material.

The Injecting Fluid.—The following mixture has succeeded admirably in my hands, and I therefore recommend it strongly. It penetrates to the finest

vessels. The specimens injected with it retain their colour perfectly, and the injected tissues can also be stained with carmine.

> Price's glycerine, 2 oz. by measure.
> Tincture of perchloride of iron, 10 drops.
> Ferrocyanide of potassium, 3 grains.
> Strong hydrochloric acid, 3 drops.
> Water, 1 oz.

Mix the tincture of iron with one ounce of the glycerine; and the ferrocyanide of potassium, first dissolved in a little water, with the other ounce. These solutions are to be mixed together very gradually in a bottle, and are to be well shaken during admixture. The iron solution must be added *to* the ferrocyanide of potassium. Lastly, the water and hydrochloric acid are to be added. Sometimes I add a little alcohol (2 drachms) to the above mixture.

This fluid does not deposit any sediment, even if kept for some time, and it appears like a blue solution when examined under high magnifying powers, in consequence of the insoluble particles of Prussian blue being so very minute.

The Carmine Fluid.—The following is the composition of the carmine fluid:

> Carmine, 10 grains.
> Strong liquor ammoniæ, ½ drachm.
> Price's glycerine, 2 ounces.
> Distilled water, 2 ounces.
> Alcohol, ½ ounce.

The carmine in small fragments is to be placed in a test tube, and the ammonia added to it. By agitation, and with the aid of the heat of a spirit-lamp, the carmine is soon dissolved. The ammoniacal solution is to be boiled for a few seconds and then allowed to cool. After the lapse of an hour, much of the excess of ammonia will have escaped. The glycerine and water may then be added and the whole passed through a filter or allowed to stand for some time, and the perfectly clear supernatant fluid poured off and kept for use. This solution will keep for months, but sometimes a little carmine is deposited, owing to the escape of ammonia, in which case one or two drops of liquor ammoniæ to the four ounces of carmine solution may be added.

The rapidity with which the colouring of a tissue immersed in this fluid takes place, depends partly upon the character of the tissue and partly upon the excess of ammonia present in the solution. If the solution be very alkaline the colouring is too intense, and much of the soft *tissue* or imperfectly developed formed material around the germinal matter, is destroyed by the action of the alkali. If, on the other hand, the reaction of the solution be neutral, the uniform staining of tissue and germinal matter may result, and the appearances from which so much is learnt are not produced. When the vessels are injected with the Prussian blue fluid the carmine fluid requires to be sufficiently alkaline to neutralise the free acid present. The permeating power of the solution is easily increased by the addition of a little more water and alcohol.

Some tissues absorb the colour very slowly. Fibrous tissue, bone and cartilage, even in very thin sections, will require twelve hours or even more,

but perfectly fresh soft embryonic tissues, and very thin sections of the liver and kidney, thin sections of morbid growths rich in cells, may be coloured in half an hour, while the cells of the above structures, placed on a glass slide, may be coloured in less than a minute. I have often coloured the germinal matter of the fresh liver cell *in a few seconds*, by simply allowing the carmine fluid to flow once over the specimen.

After the specimen has been properly stained, it is to be washed in a solution consisting of—

Strong glycerine, 2 parts.
Water, 1 part.

It is then transferred to the following acid fluid :—

Strong glycerine, 1 ounce.
Strong acetic acid, 5 drops.

After having remained in this acid fluid for three or four days, it will be found that the portions of even soft pulpy textures have regained the volume they occupied when fresh. They have swollen out again even in the strongest glycerine.

It being established as a principle that, for minute investigation, tissues must be immersed and thoroughly saturated with viscid media miscible in all proportions with water, it almost follows that reagents applied to such tissues should be dissolved in media of the same physical properties. For a long time past I have been in the habit of employing solution of potash, acetic acid, and other reagents, dissolved in glycerine instead of in water. In some cases I have found the addition of very strong solutions of certain reagents necessary. For example, the greatest advantage sometimes results from the application to a tissue of very strong acetic acid. If the acid be added to glycerine in quantity, the solution will no longer be viscid, so that another plan must be resorted to. I thicken the strongest acetic acid with sugar, a gentle heat being applied to dissolve the sugar. Thus a very strong acetic acid solution of the consistence of syrup can be most readily prepared. Strong solutions of potash, soda, and other reagents, are to be made in the same way. Thus a complete chemical examination may be conducted upon tissues, solutions, or deposits preserved in viscid media. The reactions are most conclusive, but of course take a much longer time for completion than when carried out in the ordinary manner. Ten or twelve hours must be allowed to elapse before the change is complete, and the process is expedited if the slide be placed in a warm place (about 100°).

Chromic Acid Fluid.—A most valuable fluid to the microscopist, is a solution of chromic acid in glycerine, and another solution of bichromate of potash in the same fluid. A few drops of a strong solution of chromic acid may be added, so as to give to the glycerine a pale straw colour. The bichromate of potash solution is prepared by adding from twelve to twenty drops of a strong saturated solution of bichromate of potash to an ounce of the strong glycerine. By this plan, the hardening effects of these reagents upon the finest nerve tissues are improved, while the granular appearance which is caused by aqueous solutions of these substances is much less. Sometimes advantage seems to result from mixing a little of the chromic acid with the acetic acid solution of glycerine.

If desired, sugar may be substituted for glycerine in all the fluids employed, including the carmine and injecting fluids; but glycerine, although more expensive, possesses many advantages, and, as far as I am able to judge, is the best viscid medium to employ for general purposes.

One great inconvenience of syrup arises from the growth of fungi, especially in warm weather. Camphor, creosote, carbolic acid, naphtha, prevent this to some extent; but it is a disadvantage from which strong glycerine is perfectly free. Sometimes, too, crystallisation occurs, and destroys the specimen. In using first a syrupy fluid, and then glycerine, to the same specimen, it must be remembered that the two fluids mix but slowly, so that plenty of time must be allowed for the thorough penetration of the medium used last.

I keep various tests, such as alcohol, ether, the various acids, and alkalies, and other tests in the form of viscid solutions made with glycerine or sugar. The reaction of the iodine tests for amyloid matter, starch and cellulose, is much more distinct when employed in this manner. The plan is, to allow the texture to be tested to be thoroughly saturated with the strong glycerine solutions, and then to add water. In the course of a few hours the reaction takes place very strongly.

The plan pursued for preparing the Tissue.—The general plan I follow, is the same for all tissues of all vertebrate animals and morbid growths; but I will describe the several steps of the process as they were conducted in the demonstration of the minute structure of ganglion cells, and of the structure of the papillæ of the frog's tongue.* The description given also applies to the mode of preparing specimens of muscular fibre to demonstrate the mode of distribution of the finest branches of nerve fibre, and specimens of the minute structure of the brain, spinal cord, and ganglia of man and the higher animals.

Perhaps it will be most useful to describe the mode of proceeding when a frog is to be prepared for minute inspection. My researches upon the tissues of the frog have been principally conducted upon the little green tree frog (Hyla arborea), for experience has proved to me that the tissues of this little animal are so much more favourable for investigation than those of the common frog, that it is well worth while to obtain specimens, even at the cost of 2*s.* or 2*s.* 6*d.* each. The student may, however, obtain very beautiful specimens from the common frog. The animal is killed by being dashed suddenly upon the floor, but it must first be carefully folded up in the centre of a large cloth, so that the tissues may not be bruised in the least degree. Next an opening is made in the sternum, the heart exposed, and a fine injecting pipe, after being filled with a little injection, is tied in the artery. The injection ought to be complete in from twenty minutes to half an hour, and sometimes in less time than this. The injection, being pale, cannot be very distinctly seen by the unaided eye, but if the operation has been conducted successfully, the tissues will be found swollen and the areolar tissue about the neck will be fully distended.

The injection being complete, the abdominal cavity of the frog is opened, and the viscera washed with strong glycerine. The legs may be removed, the mouth slit open upon one side, and the pharynx well washed with glycerine.

* "On the structure and formation of the so-called apolar, unipolar, and bipolar nerve cells of the frog."—Phil. Trans. May, 1863. "New Observations upon the minute anatomy of the papillæ of the frog's tongue."—Phil. Trans. June, 1864.

If it is desired to prepare one organ only, this may, of course, be removed and operated upon separately; but I generally subject the entire trunk, with all the viscera, to the action of the carmine fluid. If the brain and spinal cord are special objects of inquiry, the cranium and the spinal canal must be opened so as to expose the organs completely, before the staining process is commenced. Enough of the carmine solution is then placed in a little porcelain basin or gallypot, just sufficient to cover the entire trunk and viscera. The specimen is then moved about in the carmine fluid, so that every part that is exposed may be thoroughly wetted by it; sometimes slight pressure with the finger is required. It is left in the carmine fluid for a period varying from four to six or eight hours, being occasionally pressed and moved about during this time, so as to ensure the carmine fluid coming into contact with every part. By this time the blue colour of the vessels of the lungs, viscera, &c., will have almost entirely disappeared, and all the tissues will appear uniformly red. The staining is now complete. The carmine fluid is poured off and thrown away, and the preparation washed quickly with the glycerine solution. The specimen is now placed in another little basin, and some strong glycerine poured over it; it is then left for two or three hours, and a little more strong glycerine added; when, from six to twelve hours since the specimen was removed from the carmine solution have elapsed, the preparation is ready for the last preliminary operation. The glycerine used for washing it is poured off, and sufficient strong Price's glycerine added just to cover it. To this, three or four drops of strong acetic acid are added, and well mixed with the glycerine. In this acid fluid the preparation may be left for several days, when a small piece of some vascular part may be cut off, placed in a drop of glycerine, and subjected to microscopical examination. If the injected vessels are of a bright blue colour, and the nuclei of the tissues of a bright red, the specimen is ready for minute examination; but if the blue colour is not distinct, three or four more drops of acetic acid must be added to the glycerine, and the preparation soaked for a few days longer.

If the nuclei are of a dark red colour, and appear smooth and homogeneous, more especially if the tissue intervening between them is coloured red, the specimen has been soaked too long in the carmine fluid; but in this case, although parts upon the surface may be useless for further investigation, the tissues below may have received the proper amount of colour.

Another plan which I have adopted, and which, although more difficult in practice, if carried out with due care, possesses some advantages, is the following: The vessels are in the first instance thoroughly injected with the carmine fluid, and the preparation allowed to soak for four-and-twenty hours, when a little glycerine is first injected, and then the Prussian blue injecting fluid introduced until the capillary vessels are completely filled with it. The fluid must be injected very slowly, and but slight pressure employed, or the vessels will certainly be ruptured. When the second injection is complete, the textures required for investigation may be removed, washed in glycerine, and, after soaking for a day or two in acetic acid glycerine, will be ready for microscopic investigation. Beautiful and most perfect specimens of solid internal organs, like the brain and spinal cord, may be obtained by this process; and it is the most perfect plan I have adopted, although it presents many practical difficulties, and will probably fail in the hands of the student

unless he has the patience to make the attempt many times ; when, however, success is obtained, he is well rewarded for the trouble he has taken, and the many failures he may have experienced.

The tissues or organs to be subjected to special investigation may now be removed, and transferred to fresh glycerine ; they may be kept in little corked glass tubes, and properly labelled. Generally, the tissue will contain sufficient acetic acid, but if this is not the case, one drop more may be added.

Suppose, now, the nerves with the small vessels and areolar tissue at the posterior and lower part of the abdominal cavity, have been placed in one tube, and the prepared tongue of the Hyla in another, the former specimen may be taken out of the glycerine and spread out upon a glass slide. If it be examined with an inch power, numerous microscopic ganglia may be seen. Several of these, perhaps, are close to small arteries. Those which are most free from pigment cells are selected, and removed carefully by the aid of a sharp knife, fine scissars, forceps, and a needle point. This operation may be effected while the slide is placed upon the stage of the microscope. The *transmitted light* enables the observer to see the minute pieces very distinctly ; if necessary, a watchmaker's lens may be used. The pieces selected are transferred to a few drops of the strongest glycerine placed in a watch glass or small basin, or in one of the little china colour moulds, and left to soak for several hours.

The microscopical examination of the specimen may now be carried out. One of the small pieces is placed upon a glass slide, in a drop of fresh glycerine, and covered with thin glass. The glass slide may be gently warmed over the lamp, and the thin glass pressed down upon the preparation by slight taps with a needle point. The specimen may now be examined with a quarter, and afterwards with the twelfth of an inch object glass. A good deal of granular matter will possibly obscure the delicate points in the structure. The slide is again gently warmed, and, with the aid of a needle, the thin glass is made to slide over the surface of the specimen, without the position of the latter being altered, and then removed and cleaned. The specimen is then washed by the addition of drop after drop of strong glycerine containing five drops of acetic acid to the ounce. The slide can be slightly inclined while it is warmed gently over the lamp, in such a manner that the drops of glycerine slowly pass over the specimen and wash away the débris from its surface. The most convenient instrument for dropping the glycerine on the specimen is a little bottle, of two ounces capacity, with a syphon tube drawn to a point, and a straight tube, with an expanded upper part, over which is tied a piece of stout sheet vulcanized India-rubber. Upon compressing the air, by pressing down the India-rubber, the glycerine is forced drop by drop through the syphon tube and allowed to fall upon the specimen.*

When several drops of pure glycerine have been allowed to flow over the specimen, the thin glass cover, after having been cleaned, is re-applied and pressed upon the specimen very gradually, but more firmly than before. If

* These little bottles, as well as any other instruments or apparatus required, can be obtained of Mr. Matthews, Carey-street, Lincoln's Inn-fields ; Mr. G. King, 190, Great Portland-street, or Mr. Highley, Green-street, Leicester-square.

the preparation looks pretty clear when examined with the twelfth, the glass cover may be cemented down with Bell's cement, and the specimen left for many days in a quiet place. It may then be re-examined, the process of washing with glycerine repeated, and further pressure applied until it is rendered as thin as is desired. When this point has been reached, more glycerine with acetic acid is to be added, and a plate of mica or the *thinnest glass cover* applied, when it may be examined with the twenty-fifth. The process of flattening may be pushed still further if desirable,—and if only carried out very slowly by gentle taps or careful pressure with the finger and thumb *from day to day*, the elements of the tissues are gradually separated without being destroyed. If there be much connective tissue, which interferes with a clear view of the finest nerve or muscular fibres, it may be necessary to immerse the specimen for some days in the acetic acid syrup, and then transfer it to fresh glycerine. The success of this process depends upon the care and patience with which it is carried out. The most perfect results are obtained in cases where the washing, pressure, and warming have been very slowly conducted, and it is most interesting to notice the minute points of structure which are gradually rendered clearer by the application of a gentle heat, subjecting the specimen to a little firmer pressure or by soaking it in a little fresh glycerine placed in a watch-glass.

Specimens of tissue prepared in this way can be transferred from slide to slide, and no matter how thin they may be, after having been allowed to soak in fresh glycerine they may always be laid out again perfectly flat upon another slide, by the aid of needles.* The action of these viscid fluids is most valuable, and I feel sure that by the process here given, retaining the principle, but modifying the details in special cases, many new and important anatomical facts will be discovered. Until this process is carried out successfully by other observers, I have little hope of my own observations being confirmed.

Suppose the observer desires to study the papillæ of the frog's tongue. Small pieces of the mucous membrane being removed by sharp scissors, they are transferred to glycerine, subjected to the same very gradually increased pressure, until the individual papillæ are themselves slightly flattened. It is possible from a specimen to remove a number of the separate papillæ on a needle point, transfer them to glycerine or to the acetic acid syrup, and then mount them for examination with the $\frac{1}{25}$th object-glass. All the points I have described and figured in my paper may then be demonstrated in several papillæ.

Thin sections of brain, spinal cord, &c., may be subjected to the same process for examination with the highest powers. The tissues of man in health and disease and various morbid growths may be prepared in precisely the same manner. Even the vessels of a small portion of a solid organ, like the brain, liver, or kidney, or those of a small tumour, may be very readily injected. The escape of the injection from divided vessels may be prevented by tying them or by pressure, but considerable escape from the divided vessels does not prevent some of the capillaries being perfectly filled. The most delicate preparations retain their characters for many months, and some

* I often mount these specimens upon a circle of thin glass about $\frac{3}{4}$ of an inch in diameter, instead of upon a glass slide. The circle is then placed in a wooden slide in the centre of which a hole has been drilled of the proper dimensions to receive it. It is fixed in its place by a ring of gummed paper.

for several years, so that in many cases the very preparations from which my drawings have been made, have been preserved.

Method of preparing specimens of Bone and Teeth and other hard tissues.—By the methods generally employed for demonstrating the structure of bone, teeth, and other hard tissues, we are enabled to form a notion of the dead and dried tissue only. The soft material is dried up before the section is made.

And yet this very soft material, which is not represented in the drawings published in different works, is that which makes the only difference between the dried bone or tooth in our cabinets and that which still remains an integral part of the living body. So far from this soft matter being unimportant, it is the most important of all the structures of the hard texture. It is by this alone that all osseous and dental tissues are formed and nourished, and from the arrangement of this soft matter not having been recognized the most erroneous ideas have prevailed, and still prevail, upon the formation and nutrition of the osseous and dental tissues.

Even now it is generally believed that the dentinal tubes are real tubular passages for conveying *fluids* to all parts of the dentine, and are thus subservient to its "nutrition," and yet it is more than eight years since Mr. Tomes proved most conclusively that these so-called "tubes" were occupied in the recent state by a moist but tolerably firm material ("Phil. Trans.," Feb., 1856).

I have verified Mr. Tomes' description, and am quite certain that the so-called dentinal tubes are not channels for the mere flowing up and down of nutrient fluid.*

Suppose a tooth is to be prepared for minute microscopical investigation, we may proceed as follows. The same plan is applicable to bone and shell.

1. As soon as possible after extraction, the tooth may be broken by a hammer into fragments, so as to expose clean surfaces of the tissues. Pieces of dentine with portions of pulp still adhering to them may then be selected and immersed in the carmine fluid, and placed in a vessel lightly covered with paper, so as to exclude the dust. The whole may be left in a warm room for from twenty-four to forty-eight hours.

2. The carmine solution may then be poured off, and a little plain dilute glycerine added, as already described in the case of soft tissues.

3. After the fragments of teeth have remained in this fluid for five or six hours, the excess, now coloured with the carmine, may be poured off, and replaced by a little strong glycerine and acetic acid.

4. After having remained in this fluid for three or four days, it will be found that the portions of soft pulp have regained the volume they occupied when fresh. They have swollen out again even in the strongest glycerine.

5. I have found that in many cases, when it is desired to study the arrangement of the nerves, it is necessary to harden the pulp by immersion in glycerine solution, made by adding to an ounce of the glycerine solution of acetic acid two or three drops of a strong solution of chromic acid. The fragments may remain in this solution for three or four days, and then be transferred to the acetic acid solution, in which they may be preserved for years with all the soft parts perfect.

* On the structure of recent bone and teeth, see my lectures on "The structure and growth of the tissues." Delivered at the Royal College of Physicians, 1860.

6. The specimens are now ready for examination. Thin sections are *cut* with a knife from the fractured surfaces of the dentine, including a portion of the soft pulp. The knife should be strong, but sharp. In practice I have found the double-edged scalpels made for me by the Messrs. Weiss and Son, of the Strand, answer exceedingly well for this purpose, nor will the edge of the knife be destroyed so soon as would be supposed.

7. The minute fragments of sections thus obtained are placed upon a slide and immersed in a drop of pure strong glycerine, in which they may be allowed to soak for an hour or more, and then examined by a low power (an inch). The best pieces are then to be selected by the aid of a fine needle, and removed to a drop of glycerine containing two drops of acetic acid to the ounce, and placed upon a clean slide. Lastly the thin glass cover is carefully applied, and the specimen may be examined with higher powers.

8. If it is desired to retain the specimen, the excess of glycerine fluid is absorbed by small pieces of blotting-paper, and the glass cover cemented to the slide by carefully painting a narrow ring of Bell's cement round it. When this first thin layer is dry, the brush may be carried round a second time, and after the lapse of a few days, more may be applied. Mounted in this way the specimen will retain its character for years.

Hard tissues, like bone, dentine, and enamel, become somewhat softened by prolonged maceration in glycerine, and if a few drops of acetic acid are added, the softening process may be carried to a greater extent, and yet without the calcareous matter being dissolved out to any perceptible extent. If desired, of course the calcareous matter may be in part or entirely removed by increasing the strength of the acid fluid in which the preparation is immersed. But, far short of this, the hard, brittle texture is so altered that thin sections may be *cut* without any difficulty. Specimens prepared in this way may be examined by the highest magnifying powers yet made,—by which statement I mean, of course, to imply that more may be learned by the use of such high powers (1,000 to 3,000 linear) than by employing ordinary object glasses.

Contrary to general opinion, many of the softest textures may be investigated with the greatest facility after having been soaked in strong glycerine. In preparing these, the same steps which have been described must be carried out, but the glycerine used at first must be weaker, and its strength must be very slowly and gradually increased. Young embryos may be injected with the Prussian blue fluid. The pipe cannot be tied in the vessels, as they are extremely soft. But if it is simply inserted, much of the injection will run onwards into the capillaries, and the escape of a certain quantity by the side of the pipe is a matter of no moment.

I have beautiful preparations of the most delicate embryonic tissues, preserved in the strongest glycerine. It is often advantageous to harden the tissues slightly by the addition of a little of the chromic acid glycerine solution. When once the tissues have been fully permeated by glycerine, they may be dissected and manipulated in a manner which before was impossible.

[L. S. B.]

CHAPTER I.

OF STRUCTURE.—OF THE TISSUES GENERALLY.—OF THE CELL, OR ELEMENTARY PART.—DIFFERENT FORMS OF CELLS.—OF INTERCELLULAR SUBSTANCE.—OF THE LIVING OR GERMINAL MATTER OF THE CELL.—OF THE DEVELOPMENT AND MULTIPLICATION OF CELLS.—OF THE CHANGES IN THE CELL IN DISEASE.

In certain tissues we are unable, even with the aid of the highest powers, to demonstrate any structural peculiarities whatever. But it must be borne in mind that in some apparently perfectly homogeneous textures distinct structure may be demonstrated by special methods of investigation. Various plans of tinting have been employed for this purpose, and solutions of rosanilin dye, nitrate of silver and other soluble colouring matters have been found very useful. It is, therefore, not improbable that future research will prove that many tissues which are now considered perfectly structureless and homogeneous possess distinct structure.

The different physical properties of tissues seem to be due in part to their chemical composition and partly to peculiarities in what may be termed the build of the texture. The differences in structure and properties of the various tissues must not be attributed merely to a difference in the composition of the nutrient material which takes part in their production, for, from the same pabulum, matter different in physical properties and chemical composition may be produced through the agency of structureless living matter. Nor can we trace the cause of the difference in structure of the tissues to difference in structural character, or chemical composition of the germinal matter from which they are formed. So far from this being the case it seems that the very different textures in the body all result from changes in germinal matter having, as far as can yet be ascertained by *observation*, precisely the same characters. And we know that all the masses of germinal matter concerned in the process have the same origin. It seems, therefore, upon the whole, more probable that the masses of germinal matter of the different tissues produce from the same nutrient constituents, substances differing in composition and in texture by virtue of

some peculiar inherent power, than that each selects from a common fluid those particular materials most nearly corresponding to the substance to be formed, and causes them to combine. The constituents of the tissues are not constituents of the blood which are merely selected and separated from it, but they are actually *formed* through the agency of the germinal or living matter. The formative power of this germinal or living matter seems to be of far greater importance than its power of selection. Indeed, this supposed selective power, considered by some sufficient to account for the observed facts, has been assumed rather than proved to be one of the most important properties of the cell.

Granules, Globules, Fibres, Membranes.—In certain textures, and suspended in the fluids of the animal body, different structural elements may be observed which have received definite names. *Granules* are minute particles which exhibit no definite form or magnitude when examined under very high magnifying powers. Granules are represented in plate I. fig. 1. *Globules* are small bodies of spherical or oval form, composed throughout of the same substance, exhibiting a clear centre and a distinct outline, the apparent thickness of which varies according as the medium in which the globule is placed differs in refractive power from the material of which the globule itself is composed. So that the outline of the same globule may appear to be *very thick and black* in water, and *as a very thin line* in oil, turpentine, or Canada balsam. Granules and globules vary in chemical composition. They may be composed of *albuminous matter*, *fatty matter*, or *earthy matter*, and these substances may be distinguished by the application of chemical tests.* Globules are represented in plate I. fig. 2. A very good idea of the general appearance of globules may be formed by examining a drop of milk under a magnifying power of 200 diameters.

Fibres may appear as exceedingly fine *lines*, the diameter of which cannot be measured, or as distinct *cylindrical threads*, or *flattened bands*, having a definite diameter. The fibres may be straight, or wavy, or much curved. They may be arranged parallel to one another or they may cross one another at every

* Globules of albuminous matter are rendered transparent by acetic acid and are dissolved by potash and soda. Fat globules are soluble in ether and not altered by acetic acid. Globules of earthy matter are dissolved by acids but are not changed by alkalies.

possible angle. Not unfrequently there is an indication of fine lines although no distinct fibres separable from one another can be demonstrated. This is spoken of as a fibrous appearance as is represented in fibrous tissue, plate I. fig. 3 *a*.

Membrane.—Membrane may be so perfectly transparent and homogeneous that we are only able to demonstrate its existence by the plaits or folds which it forms. Sometimes membrane appears granular or exhibits a fibrous appearance, and not unfrequently calcareous particles are deposited in its substance. Membrane sometimes consists of an insoluble material allied to albumen, but some membranes are composed of a substance which in its physical and chemical characters agrees with yellow elastic tissue. Clear, transparent, and structureless membrane is represented in plate I. fig. 4.

OF THE TISSUES.

Although fully developed tissues might be classified according to the peculiarities of structure they exhibit, the classification would be defective in so many particulars that little advantage could result from the attempt to arrange the tissues of man or those of animals and plants in several artificial groups. Nevertheless such an arrangement as that given below, though far from perfect, may be of some assistance to the student:—

TABULAR VIEW OF THE TISSUES OF THE HUMAN BODY.

1. Simple membrane, homogeneous, or nearly so, employed alone, or in the formation of compound membranes.	Examples.—Posterior layer of the cornea.—Capsule of the lens.—Sarcolemma of muscle.
2. Filamentous tissues, the elements of which are real or apparent filaments.	White and yellow fibrous tissues.—Areolar or connective tissue.
3. Compound membranes, composed in some cases, of simple membrane, and a layer of cells, of various forms (epithelium or epidermis), in others of areolar or connective tissue and epithelium only.	Mucous membrane.—Skin.—True or secreting glands.—Serous and synovial membranes.
4. Tissues which exhibit a cellular structure in their fully developed state.	Cuticle. Nails. Hair.—Gland, pigment, and fat cells.—Cartilage.
5. Tissues hardened by calcareous salts.	Bone.—Teeth.
6. Compound tissues.	
a. Composed of two different kinds of tissues of simple structure.	Connective tissue.—Fibro-cartilage. Certain forms of elastic tissue.
b. Tissues composed of material which possesses special endowments.	Muscle.—Nerve.
c. Tubes for distributing nutrient matter.	Blood vessels.—Absorbent vessels.

Of the Tissues generally.—The first texture enumerated in this table is an example of the simplest form of membrane. Its principal character is extension; but as to the arrangement of its ultimate particles nothing is known; for, under the highest powers of the microscope it appears homogeneous, that is, without visible limits to its particles, or, at most, irregularly and very indistinctly granular. The capsule of the lens, the posterior layer of the cornea, the uriniferous tubes, and the walls of many "cells" are composed of it; and it enters into the formation of muscle, nerve, and the adipose and tegumentary tissues. It is not peculiar to living beings, for a structureless fibre or membrane may be produced artificially.

The filamentous tissues are extensively used for connecting different parts, or for associating the elements of other tissues. The ligaments of joints, for instance, are composed of the white or yellow fibrous tissues; and areolar or connective tissue surrounds and connects the elementary parts of nerves and muscles, accompanies and supports the blood-vessels, and unites the tegumentary tissues to their subjacent parts or organs.

Under the title *compound membranes* we include those expansions, which form the external integument of the body, and are continued into the various internal passages, which, by their involutions, contribute to form the various secreting organs or glands. These are composed of the simple homogeneous membrane, covered by epidermis or epithelium, and resting upon a layer of vessels, nerves, and areolar tissue in great variety; and they constitute the skin, and mucous membranes, with the various glandular organs which open upon their surface.

To these, we may add those remarkable membranes, composed of areolar tissue and a thin indusium of epithelium, which are employed as mechanical aids to motion. These are the serous membranes which line the great cavities of the body, and the synovial membranes, which are interposed between the articular extremities of the bones in certain joints, or are connected with and facilitate the motions of tendons.

The tissues which compose the fourth class have no common character, except their adherence, in the adult state, to the primitive cellular structure, and their analogy in that particular with the vegetable tissue. Although a certain agreement, in morphological characters, allows these textures to be grouped

together, none can be more dissimilar as regards their endowments. They differ materially as to the degree of cohesion between their cells: in cartilage there is generally what is spoken of as a firm and resisting intercellular substance, which, however, is not truly *inter*cellular, since it exactly corresponds to what in other tissues is spoken of as cell-wall.

The sclerous tissue (σκληρος, hard,) contains a large proportion of inorganic material, to which it owes its hardness.

The compound tissues are those, the elementary parts of which are concerned in the production of two distinct tissues. Fibro-cartilage is a compound texture, being made up of white fibrous tissue and cartilage; it is employed almost exclusively in the mechanism of the joints of the skeleton, in which it is associated with bone, cartilage, and ligaments.

Muscle and nerve are composed of parallel fibres or threads, each fibre being compound, and exhibiting a special structure; in muscle, it is composed of homogeneous membrane, disposed like a tube, containing a fleshy (*sarcous*) substance, arranged in a particular manner, which is the seat of the peculiar contractile properties of the tissue; and, in nerve, the fibres are composed of similar tubes of homogeneous membrane containing an oleo-albuminous substance, within which is a delicate band or fibre possessing the remarkable property of conducting the nerve force. The arteries, veins, and larger absorbent vessels, are also examples of compound tissues,—their walls being composed of several textures exhibiting different endowments.

All these different tissues, however, possess in the living growing state, disseminated at nearly equal distances through their substance, masses of germinal or living matter, which appear perfectly colourless, homogeneous, and almost diffluent. In this material all the essential changes take place. Each mass is spherical or oval in form, and often exhibits in its substance one or more smaller masses (nuclei), which are somewhat less transparent than the general mass in which they are embedded. In the nuclei in many cases are other still smaller masses (nucleoli), and sometimes within these yet another series may be detected with the aid of very high magnifying powers. Thus it would seem as if centres were arranged within centres.

Although the various tissues existing in the fully developed organism differ remarkably from one another in structure, physical properties, chemical composition, and action, they all pass through a similar series of changes during their formation. The production of the matter of which the outer part of the simple cell of mildew is composed, is the result of changes probably very similar in essential nature to those which end in the production of the highest and most complex cell in the nervous system of man, and, when successive layers are to be demonstrated in the outer part of any cell, as is often the case, they have been deposited in the same order. We are as ignorant of the real cause and of the nature of the one process as the other. But it is reasonable to infer that if we could ascertain the nature of the changes which actually take place in the simplest living beings during their growth and multiplication, the modifications which occur in the most complex would very soon be understood.

Although we cannot understand or explain how phenomena, which we can observe without difficulty, result, we can demonstrate certain facts, in connection with cell formation, of the utmost interest. We may infer the course taken by the lifeless nutrient material when it is absorbed by the living elementary part or cell, because we can see coloured fluid pursuing the same course when the cell is even detached from the living body and placed under our microscopes. We can show where the inanimate pabulum becomes changed and acquires new and wonderful properties which in turn it can communicate to new inanimate matter. We can observe actions in this altered matter which we cannot explain, but which we may with reason refer to these newly-acquired powers; the actions and changes which take place in this matter are very different to anything familiar to us apart from living beings, and hence to these we limit the term *vital*. We can demonstrate where the *tissue* is first produced, and the precise position in which new tissue is added to that which already exists. We can show which is the youngest and which is the oldest portion of a tissue, and we can give some explanation of the mode in which the old tissue which has done its work is destroyed and removed. Lastly, in certain cases we can show how, after the old tissue has been removed, new and more complex structure takes its

place. In short, we possess observations sufficiently complete, in some instances, to enable us to sketch, imperfectly it is true, the life history of the texture, and give an account of its development, the changes occurring in it during its fully-developed state, its gradual decay and removal, and the manner in which its place is occupied by new tissue. We can also trace in some instances the modifications occurring in these processes under certain altered and exceptional conditions which constitute disease.

OF THE CELL, OR ELEMENTARY PART.

Of the Cell.—The cell is even now considered by many to be a body consisting of certain essential definite and constant parts (*cell wall*, *cell contents*, and *nucleus*), to each of which a special office has been assigned by some writers. Some have supposed that living cells exert an influence upon matter which surrounds them, or even upon other living cells at a distance from them. Others maintain that very active powers of producing chemical and other changes reside in the *nucleus* alone. The power of producing change has been attributed in turn to the cell wall, to the matter within the cell, and to the intercellular substance. No well-ascertained facts have, however, yet been adduced in favour of the view, that any living structure whatever can influence matter at a distance from it, so as to alter its properties or composition, or in support of the notion that cell wall, cell contents, or intercellular substance possess any metabolic power whatever. The power of effecting changes in some mysterious or at least unexplained manner, has, however, been assumed to exist in the cell even by some of those observers who have most strongly advocated the physical views of life.

On the other hand, the wonderful changes occurring in the development of tissues have been spoken of as if they could be very readily imitated artificially. The formation of a cell tissue has been compared to the formation of a wall in which ready-made bricks (cells) are supposed to be cemented together by ready-made mortar (intercellular substance). The formation of the tissue has been described as if the cells were first formed and then arranged in their places, and the intercellular sub-

stance deposited between them. But how different is the process in nature! At first there are no cells at all. There are but small masses of transparent living germinal matter separated from one another by a little soft formed matter. From this anatomically simple material the fully formed tissue results by gradual changes. New masses of germinal matter are produced by the division and multiplication of those existing before, in the manner represented in figs. 5 and 6. New formed material is formed from these, and as they separate or move away from one another, it accumulates in the intervals between them. The relative proportion which the latter bears to the germinal matter gradually increases as the tissue advances towards its perfect state of development. See figs. 7 and 8. The changes go on in regular order uninterruptedly from the earliest period when there was nothing but a little formless, structureless living matter, till the tissue or organ is formed, and its structure fully developed.

It has been inferred by many writers, that in the formation of a fibre, elongated cells become joined together, and it has been supposed that in the production of a tube the walls of several cells coalesce, and thus the cavity of the resulting tube corresponds to the cavities of the original cells. In the formation of such a tissue as muscle or nerve, it has been assumed that the outer or membranous sheath is formed by coalescence of *cell walls;* while the proper material (contractile tissue, or nerve fibre) is supposed to result from a modification occurring in the cell contents. When processes are seen to project from cells, it is said that they have been *shot out* or protruded from the cell; while, in a tissue composed of stellate cells, authorities have accounted for the arrangement by supposing that the tubular processes of contiguous cells grew away till they met one another, and that when they met they coalesced, so that the cavity of one cell became connected with the cavities of neighbouring cells by tubular communicating channels. And yet no one has even attempted to explain how it happens that the processes or tubes supposed to grow from contiguous cells invariably manage to hit one another exactly, to meet, join, and at last to coalesce, without in any instance overlapping one another, or ever failing to meet in the exact line. But if we examine such a tissue at an early period of its development, we find that

so far from there being any indications of cells from which outgrowths are formed, the masses of germinal matter are continuous with one another; so that, in fact, the connecting processes or tubes are connected from the first, and, as growth takes place, the connecting tubes become thinner and thinner, being as it were gradually drawn out as the masses of germinal matter become separated farther and farther from one another, in the manner shown in figs. 11, 12, 13, and 14.

Careful observation of one particular tissue at different periods of its growth will convince the observer that its formation takes place in a very simple manner, and that the formation of all tissues exhibits much in common. At no period of the life of many tissues can the arbitrary definition usually given to the cell (cell wall, cell contents, and nucleus) be correctly applied to the elementary parts of which the texture is composed, nor in any case are such bodies first produced and then arranged in special positions and united together with a connective substance so as to form a mass of tissue.

Nevertheless the term "cell" is short and convenient, and it may be still applied to the anatomical elementary part of every tissue at every period of its life, if the meaning be slightly modified. Instead of attempting to divide the cell itself into anatomical constituents, we may speak of it as consisting of matter in two very different states or stages of existence—matter which *lives* (*germinal matter*) and matter which is *formed* and has ceased to manifest purely *vital phenomena* (formed material) (see Introduction, page 11). The simplest and most minute living particle as well as the most complex cell capable of growth or multiplication consists of matter in these two states, but the relative proportions vary greatly at different periods in the life of the cell and under different conditions.

The physical and chemical properties of the formed material differ remarkably in different cases. In one case the formed material may be perfectly fluid, in another soft and viscid, in another of intense hardness, and in some tissues a comparatively soft formed material is rendered very hard by being infiltrated with calcareous or siliceous matter.

We shall now briefly describe the general structure of the principal varieties of cells at different periods of their life, and endeavour to show how the fully developed forms in different

GRANULES, GLOBULES, FIBRES, AND CELLS OR ELEMENTARY PARTS.

Fig. 1.

Granules p. 69.

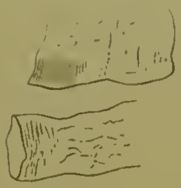
Fig. 2.

Globules p. 69.

Fig. 3.

Fibrous appearance. Fibres p. 69.

Fig. 4.



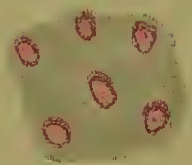
Membrane p. 70.

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 8.



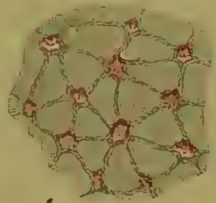
Complete division and sub-division of germinal matter, as in cartilage, and the formation of formed material. The space occupied by the three last drawings should be much larger than is represented. p. 75.

Fig. 9.

Fig. 10.

Fig. 11.

Fig. 12.



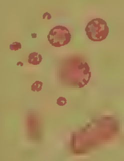
[illegible] sub-division of germinal matter as in the production of a tissue with stellate c[illegible] (. [illegible] figs. 35 & 36). Each mass for a considerable time retains its connection with the other matter,—thus are formed the 'communicating tubes' of some tissues. The space occupied by the three last Figures should be much larger than is represented. p. 76.

Fig. 13.

Fig. 14.

Subdivision of masses of germinal matter in one direction, showing how tubes and threads or filaments, differing from the ordinary formed material, may be produced. p. 76.

Fig. 15.



[illegible] particles [illegible] matter, of [illegible] mildew vi[illegible] [illegible] of an [illegible] [illegible] p. 77.

Fig. 16.

Production of formed material upon the surface of the germinal matter of mildew. × 1800. p. 77.

Fig. 17.

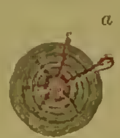


Fig. 18.

Further production of formed material in ordinary mildew. At *a*, a bud is formed by the passage of some of the germinal matter through pores in the very thick layer of formed material. × 1800. p. 78.

textures which exhibit such remarkable varieties of structure and arrangement, result.

Of the structure and formation of the simple Cell.—The low microscopic fungus which is known as common mildew is one of the simplest living things we are acquainted with, and well adapted for study. Some of the smallest particles of mildew capable of independent existence are represented in Plate I. figs 15 and 16, magnified 1800 diameters. The earliest condition of such a particle is shown in fig. 15. If the external membranous investment of a fully developed spore, or of any of the growing branches (figs. 16, 17, 18, 19) was ruptured, such minute particles would be set free in vast numbers and they constitute the living, growing matter, which may be coloured with carmine, while the envelope, or outer part of the cells, does not become coloured.

The surface of such a minute living particle becomes altered the instant it comes into contact with air or water. A thin layer upon the outer part of the particle is changed into a soft, passive, transparent, homogeneous substance, exhibiting a membranous character (cell wall), and this henceforth protects the matter within, and at the same time, being permeable to fluids, nutrient matter passes through it into the interior and undergoes conversion into living matter, which thus increases. The entire mass becomes larger. But this increase in size, it must be distinctly observed, is due not to the addition of new matter upon the *external surface*, but to the introduction of new matter into the *interior*. From this it follows that as the mass increases in size the external membrane already formed must be stretched and rendered thinner; indeed it would ultimately rupture were it not that the same conditions which led to its production cause the formation of more new material of the same kind, which is continually added within that first produced. Thus the external membranous covering is preserved, and in many cases very much strengthened by the new layers which are added. This process much resembles that by which upon a much larger scale the soft skins or hard shells of fruits are produced, and the rosy streaks upon the green covering of a young apple probably mark the tissue which was first produced, although blending so completely with the green portions which are probably of more recent formation.

From what has been already remarked it will have been inferred that the thickness which the formed material or cell membrane attains is determined mainly by the external circumstances to which the living matter is exposed. If pabulum be abundant and external conditions (temperature, moisture, &c.) favourable, it passes through the thin external membrane and the living matter increases rapidly. If, on the other hand, external conditions be unfavourable, a less proportion of pabulum passes through the membrane, and at the same time the unfavourable conditions cause the death of the living matter within, layer after layer, until at last such a condition as that represented in figs. 17 and 18 results. It will be observed that the living matter is now reduced to a very small quantity and that the less this becomes, the more strongly is that which remains protected by the increasing thickness of the envelope.

Now, if the cell in the state above referred to be exposed to the influence of a moderate temperature and moist atmosphere, and be placed under circumstances favourable to growth, the external membrane will become softened and expand. Under the influence of heat and moisture, the hard tissue will be rendered more readily permeable, and pabulum will reach the germinal matter in the interior more easily. The proportion of living matter increases, and portions make their way through natural pores now opened, fig. 17, or through chance fissures in the softened envelope, and protrude from the free surface, fig. 18. A very thin layer of the formed matter being produced on the surface of these protrusions, they are freely supplied with pabulum, which readily permeates the thin layers of formed material, and grow very quickly; and a vast extent of vegetable tissue may be produced, from what was at first a very minute particle of living matter, figs. 17, 19.

From the above observations it seems clear that the formed material of which the envelope is composed results from the death of the living matter. This passive formed material was, in fact, once germinal matter, and in many structures, especially at an early period of development, we may demonstrate the continuity of the germinal matter with the formed material. The successive layers of formed material are often very distinctly seen in vegetable tissues, as, for example, in the sea-weed, fig. 21. The oldest tissue is most external, and this now dead

tissue, is already being appropriated by organisms of another kind which are growing upon the surface, while within it passes uninterruptedly into the germinal matter. Moreover from these observations it also appears certain that the living or germinal matter is alone concerned in the active changes which take place.

It may, therefore, be concluded that the smallest independent particle which exhibits vital phenomena consists partly of matter which is lifeless, but which at an earlier period was alive, and partly of matter which lives. If but the smallest particle of the latter remains in a living state, any amount of living matter, and afterwards of lifeless tissue or formed material, may result. But if, on the other hand, all the living matter be dead, and only formed material remain, this is quite incompetent to exhibit the phenomenon of increase. In fact it does not live, it does not manifest any vital properties or powers, and although it is certain that living matter must have existed a short time previously, the formed matter has ceased to live, and can never again acquire the properties it has lost.

Epithelial Cells.—Epithelial cells from the surface of the human tongue are represented in various stages of existence in figs. 20, *a*, *b*, *c*, and 22, *a*, *b*, *c*, *d*. At first there is but a very thin layer of soft formed material upon the surface of the germinal matter, Fig. 20 *a*. The latter may divide, and each of the portions resulting would be invested with a layer of this soft formed material. Thus the "cells" may increase in number. Each increases in size in consequence of the absorption of nutrient pabulum, which passes through the layer of formed material, as in the case of the mildew, into the germinal matter. Thus the latter increases. But at the same time a portion of the germinal matter undergoes conversion into formed material, which accumulates, and as each new layer is formed upon the surface of the germinal matter, those layers of formed material already produced are stretched, and more or less incorporated with that last developed, fig. 20, *b* and *c*. For a time the germinal matter increases, while at the same time new formed material is produced. Both the constituent parts of the entire cell increase in amount up to a certain period of its life, fig. 22, *a*, *b*, *c*, but as new cells continue to be produced below, the cells already formed are gradually removed farther and farther from

the vascular surface, while at the same time their formed material becomes more condensed and less permeable to nutrient matter. Hence each entire cell ceases to increase in size. But as the mass of germinal matter still undergoes conversion into formed material, it becomes smaller as the cell advances in age, fig. 22, *d*. So that it is possible to judge of the age of a cell, irrespective of its size, by the relative amount of its component substances. In old cells there is much formed material in proportion to the germinal matter, while young cells seem to be composed almost entirely of the latter substance. In very old cells the small portion of germinal matter still unconverted into formed material, dies, and the cell having by this time arrived at the surface, is cast off, a mass of perfectly passive lifeless formed material.

It must not, however, be supposed, that formed material always exhibits the firm character of that present in the epithelial cell upon the surface of the skin and some mucous membranes. Soluble formed material may be produced in vast quantity from certain cells, which appear to undergo but very slight change. Liver cells are represented in fig. 23, *a*, *b*, *c*, *d*. These, in health, are surrounded with a thick layer of very soft formed material, the outer part of which is gradually becoming dissolved and disintegrated, and probably oxidised; part passes off in the form of very soluble biliary constituents, while part is resolved into the albuminous matter of the cell, and amyloid matter, which probably in part becomes converted into sugar. Still even in this case, there is a formation of new cells and a casting off of old ones, proceeding in the same definite direction as in the case of the epithelium of the surface, but each individual cell, probably, lives for a much longer period of time.

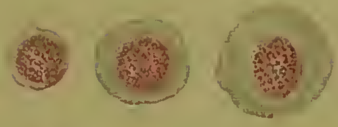
In figs. 24, 25 and 26, columnar cells of epithelium are represented. The one from the mouth of the snake, in fig. 24, takes part in the secretion of that slimy mucus which is formed in such abundance in the mouths of many reptiles. Nutrient matter is taken up from the blood by the deep surface of the cell. This becomes living matter, and some of the particles of the latter upon the distal aspect, at *a*, become formed material, which pushes that which was produced before it, towards the mouth of the cell, at *b*. Straight lines are seen passing towards the extremity, and the movement of the particles, and

GERMINAL OR L[illegible], AND FORMED, MATTE[illegible] THE CELL.

Fig. 19.

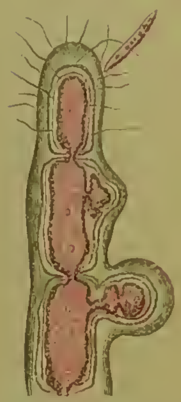
[illegible] of germinal ma[illegible] [illegible] and [illegible] [illegible] of formed [illegible] on germinal [illegible]. *a* [illegible] the manner [illegible] [illegible] × 1800. p. 78.

Fig. 20.



Production and accumulation of formed material upon the surface of germinal matter in an epithelial cell, as in cuticle. × 700. p. 79.

Fig. 21.

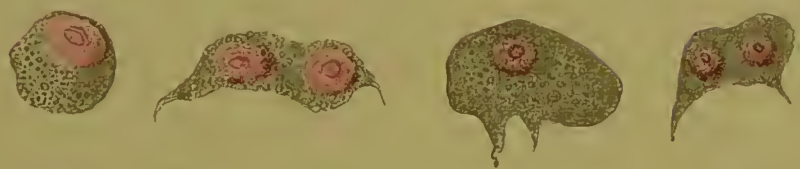


Growing extremity of the stem of a sea-weed showing the manner in which the germinal matter divides and the production of formed material, layer with in layer, upon its surface. The outermost layer is the oldest, and is undergoing disintegration. × 300. p. 78.

Fig. 22.

Drawings illustrating the production of formed material from the germinal matter in epithelial cells. p. 79.

Fig. 23.



Liver cells in different stages of [illegible] with showing germinal matter and the production of soft formed material, which becomes resolved into several different substances (fatty, amyloid, albuminous, and biliary matters). Human subject. × 700. p. 80.

Fig. 24.

[illegible] of [illegible] showing germinal [illegible] and the formed material [illegible] the [illegible]. The lower [illegible] shows the direction in which [illegible] flows towards [illegible] germinal matter, the upper one [illegible] by the formed material [illegible] from the germinal matter. p. 81.

Fig. 25.

[illegible] Cells from the fauces of a boa. × 700. p. 80.

Fig. 26.

[illegible] Epithelial cells from the [illegible] intestine of a dog showing the position of the germinal matter. *a* the layer of highly refracting matter upon the surface. × 700. p. 81.

the flow of nutrient matter, takes place constantly in one definite direction, as shown by the arrows. These mucus-forming cells are seen amongst the ciliated epithelial cells upon the tongue of the frog, and are very large and distinct upon the mucous membrane of the mouth of serpents, plate II, fig. 25*a*. It seems probable that the products of secretion from these cells are wafted away by the vibration of the cilia of the adjacent cells, as they issue from the open end of the cell in which they were produced.

In the case of the columnar cells covering the villi, lines are also seen, and probably depend upon the nutrient matter in the intestine being drawn towards the germinal matter of the cell in a linear direction (fig. 26*a*). These lines have been regarded by Kölliker and others, as *pores* in the layer of thick transparent material which seems to close what has been regarded as the free end of the cell, and it has been supposed that the fatty matter reduced to a state of very minute division by the process of digestion, passes through the pores in its way towards the lacteal; but from the circumstance that this thick transparent matter forms in some cases a continuous layer over the free extremity of the cells, from which it may be peeled off, and the fact that it varies very much in thickness at different periods of the digestive process, it seems probable that the material in question is not a part of the cell at all, but is merely deposited from the contents of the intestine, and caused to collect upon the free ends of the cells, perhaps by the currents of fluid which flow towards the "nucleus." The fluid passing constantly in the same direction would slowly dissolve the precipitated matter, and it would thus be transmitted to the germinal matter in the cell. That part of the germinal matter directed towards the opposite or attached extremity of the cell, would at the same time undergo change, and become converted into substances which would pass to the lacteal vessels upon the surface of the villus.

The different position of the mass of germinal matter in these columnar cells, and those mucus-secreting columnar cells from the frog's or serpent's mouth, should be noticed. In the intestinal cells, the pabulum flows *from* the free surface *towards* the attached extremity of the cells, but in the mucus-secreting cells it flows in the opposite direction, and it seems not im-

probable that the different situation of the germinal matter in the two classes of cells may be determined by the difference in the position of the pabulum in the two cases, figs. 25, 26*b*.

Many of the radiating lines apparent in cells seem to be due partly to the course taken by the pabulum as it flows in converging lines towards the germinal matter, and partly to the manner in which the formed material is deposited layer within layer. In large masses of germinal matter fissures or channels are sometimes seen by which the whole is mapped out into a number of smaller portions, each one of which will be bathed by the fluid as it passes along the channels. An example of the appearance alluded to is represented in plate III, fig. 27. In vegetable cells matter is deposited layer within layer, so as to thicken and strengthen the cell. This matter is, however, not deposited uniformly in every part, but the deposition is almost entirely prevented in the course taken by the currents of nutrient fluid which are continually flowing towards the germinal matter in the centre. As the process of deposition goes on, the channels gradually become narrower, but, as would be inferred, they are, except in very old cells, invariably of considerable width nearest to the germinal matter, and the "cavity" of the cell, after the drying up of the germinal matter, exhibits a stellate form, fig. 28. In fig. 32 is a portion of the thickened wall of one of the large cells in the potato which are destitute of starch, seen in fig. 31, under low power. These figures illustrate the same point.

Cells or Elementary Parts consisting of two or more kinds of formed material,—Cell-Wall and Cell-Contents.—In the mucus-secreting cells referred to in the last section, two kinds of formed material were produced from the original germinal matter of the cell, 1, that which has been called *cell-wall*, and 2, the peculiar matter found in the interior usually termed *cell-contents*. In plate III, fig. 29, are represented some of the young starch-holding cells of the potato. The so-called cell-wall is formed around, and now invests, the germinal matter, while the starch is deposited as small insoluble particles *in its substance*. In fact by the death of particles upon the surface of the living matter, the *cellulose* "cell-wall" is produced, while, in consequence of the death of some of the particles further inwards, and therefore under different conditions, *starch* results.

As the starch-holding cells increase in size, the starch granules become enlarged by deposition of layer after layer *upon their external* surface. They still lie embedded in the germinal matter, and are separated from the cell-wall by it. This outer portion of the germinal matter is known as the "*primordial utricle*" of the vegetable cell, *see* fig. 30. That the formation of the starch granules is a process closely allied to the production of the cell-wall seems proved by the circumstance that in some of the cells no starch is found in the interior, but the wall of the cell is greatly thickened by the deposition of a closely allied, but not identical material upon its internal surface, layer within layer, as represented in figs. 31 and 32.

The fat cell, or adipose vesicle, is formed in precisely the same way, and fat may be deposited amongst the germinal matter of other cells, such as the cartilage cell, and in nerve and other elementary parts in certain cases. The formation of fat in a fat cell, at different stages of development, is represented in plate III, fig. 33, *a*, *b*, *c*.

Of Stellate Cells.—It has often been said that a cell *sends* or *shoots out* branches or processes at different parts of its circumference, and thus becomes star-shaped. The processes of stellate cells are, however, never formed by any such process of growing or shooting "outwards" from the body of the cell. They are not as it were *out-growths*, which proceed from one cell and meet those protruded from neighbouring cells, but the processes are drawn out as the masses originally close together become separated, in the manner already referred to in page 75, and represented diagrammatically in plate I, figs. 9 to 12. These diagrams are not, however, strictly true, for figs. 11 and 12 would really extend over a much larger space than in the drawing, for each of the numerous masses of germinal matter in figs. 7, 8, 11 and 12, corresponds to the larger masses seen in figs. 5, 6, 9, and 10. The large pigment cells of the frog and other batrachia, and those forming the outer layer of the choroidal coat of the eye (lamina fusca), are good examples of stellate cells. The former will be found in chap. III, the latter in plate III, fig. 34.

Upon the surface of the fang of the tooth, in contact with the cementum or crusta petrosa, is a tissue of a very interesting structure, which takes part in the formation of the cementum.

It is composed entirely of branching cells, and is a most perfect example of a tissue consisting entirely of cells, the cavities of which, up to a certain period of development, *communicate with one another by tubes.* The stellate cells are here as distinct as they are in the pith of a rush. These cells and tubes do not, however, constitute an elaborate system of channels for the distribution of nutrient material to the tissue which intervenes between them, as Virchow and his school maintain. The structure is represented in plate III, fig. 35.

But perhaps the most remarkable instance of the formation of fibres by the gradual separation of cells from one another occurs in the central organs of the nervous system. The fibres are structurally continuous with the body of the cell, and become drawn out as it were, as the cells, originally continuous, become separated further and further from each other. At an early period of development the caudate cells in the cord and brain of man and animals, are represented by small and perfectly spherical cells, which lie close to one another. The small quantity of formed material between them is so transparent that no structure can be discerned in it. As yet it exhibits no indications of fibres. It is, however, very probable that fibres exist even at this early period, but their transparency and delicacy of structure render them invisible. As development advances, the masses of germinal matter become separated from one another, while at the same time they increase in size, and the fibres, which, with the outer part of the cell, constitute the formed material, become more and more drawn out in every part of their course, until they are so very thin as not to be recognizable without the use of very high magnifying powers, and a special method of preparation. The numerous interlacing nerve fibres, of which the matter intervening between the cells of the adult brain and spinal cord is almost entirely composed, are thus formed. *See* fig. 36, plate III.

Of Spherical and Oval Nerve Cells.—A cell of highly complex structure connected with the sympathetic of the frog, is represented in plate IV, fig. 40, but the manner in which this is produced will probably be understood if the principles already advanced have been carefully considered. This "cell" exhibits two fibres proceeding from it, one being coiled spirally round the other. At an early period of development it consists only

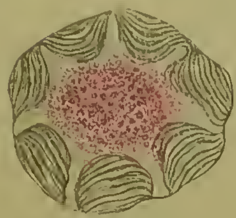
GERMINAL OR LIVING, AND FORMED, MATTER OF THE CELL.

Fig. 27.

[illegible] Cornea of the Salamander

× 700 p 82.

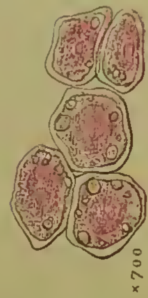
Fig. 28.



Vegetable cell, showing the manner in which secondary deposits are formed, and how the channels through which currents flow towards the 'nucleus' result

p 82

Fig. 29.



Five young starch holding cells of the potato, showing GERMINAL MATTER, with small starch globules precipitated amongst it.

× 700. p. 82.

Fig. 30.

[illegible] formed starch holding cell of the potato.

× 350 p 83

Fig. 31.

One of the large cells with thick walls from the potato, containing very little starch

p. 82

Fig. 32.

A portion of the wall of one of the cells in Fig 31, showing how the wall is thickened by the deposition of layer within layer.

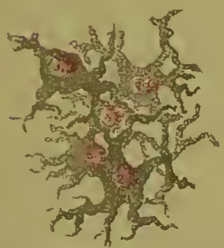
× 700. p. 82

Fig. 33.

'Fat Cells,' showing the seat of formation of the fat (formed material), and the changes occurring in the cell as it advances towards its fully developed state. Frog.

× 700 p 83.

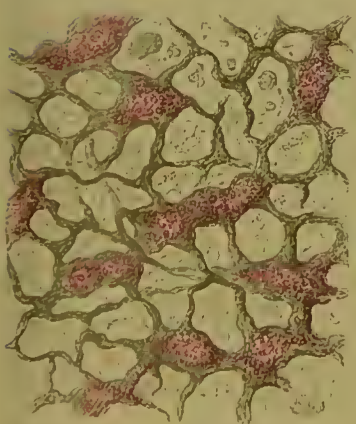
Fig. 34.



Pigment cells from the outer part of the choroid. Human

× 130. p 83.

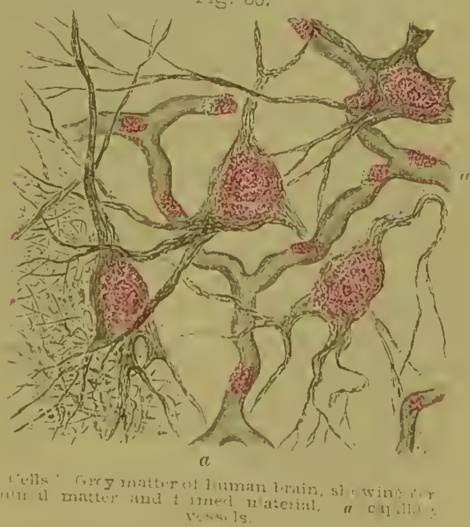
Fig. 35.



[illegible] tissue on surface of [illegible]

× 700. p 81

Fig. 36.



Cells of Grey matter of human brain, showing germinal matter and formed material. a capillary vessels.

× 350. p 81

[L. S. B.]

[To face p]

of an oval mass of germinal matter, with either extremity of which a fibre is connected. The cell moves in a direction more or less at right angles to the line of the fibres, and as it moves it probably turns round upon its own axis, in such a way that one fibre becomes coiled round the other, as represented in the drawing. This interesting form of cell will be described in the chapter upon the anatomy of nervous tissue, and it is only alluded to here as an illustration of the fact that every highly complex cell, like cells of very simple structure, consists of germinal matter and formed material. In the sympathetic ganglia of the higher vertebrata the cells are more spherical and several fibres come off from each cell, but the peculiar twisting of one fibre round the other, as in the case of the cells from the frog, and some other batrachia, has not been observed.

Of the so-called Intercellular Substance.—In cartilage, tendon, and some other tissues there is no line of separation between the portions of formed material which belong to each respective mass of germinal matter as is the case in epithelium, but the formed material throughout the entire tissue forms a continuous mass of tissue, matrix, or, as it has been termed, connective substance. From the apparent essential difference in structure, it has been supposed that tissues of this character were developed upon a principle very different to that upon which epithelial structures were produced. It has been maintained by some that in cartilage a cell-wall, distinct from the intervening transparent material, existed around each cell, and it has been very generally concluded that the matrix was deposited between the cells, and hence this was called "*inter*cellular substance."

By reference to figs. 37 and 39, plate IV, it will be seen, however, that the so-called *intercellular substance* of cartilage and tendon exactly corresponds to the formed material of the epithelial cell, fig. 22, plate II.

A "cell," or elementary part of fully formed cartilage and tendon, consists of a mass of germinal matter with a proportion of the formed material around it. A line passing midway between the different masses of germinal matter would mark roughly the point to which the formed material corresponding to each particular mass of germinal matter extended,

and this would correspond with the outer part of the surface or boundary of the epithelial cell.

In order to understand the true relation of the so-called intercellular substance of the cartilage and tendon to the masses of germinal matter, it is necessary to study the tissue at different ages. At an early period of development these tissues appear to consist of masses of germinal matter only. As development advances, the formed material increases, and the masses of germinal matter become separated further and further from one another. The appearances of a cell-wall around the germinal matter in the fully-formed tissue, and other alterations which occur, and anomalous appearances which often result as age advances, can be even more readily understood upon the view here advanced, than upon the intercellular substance theory which has been so strongly supported by some observers.

The above conclusions may be confirmed by a careful examination of white fibrous tissue. If equal portions of fœtal and adult tendon be examined, the proportion of germinal matter in each will be found to be very different. There may be five or six times as much germinal matter in a certain bulk of fœtal, as in the same bulk of fully formed tendon. The tendinous matter or tissue possesses no power of absorbing nutritive material and converting it into tissue like itself. All additions to its substance take place at those points only at which germinal matter exists. Young tendon grows much faster than fully formed tendon, and in old tendon the masses of germinal matter have become reduced to very thin lines. In figs. 38 and 39, plate IV, specimens of fœtal and fully developed tendon, from the kitten and cat, are represented.

Of the Formation of the Contractile Tissue of Muscle.—A muscle "cell" or elementary part, will consist, like that of cartilage and tendon, of the so-called nucleus, with a portion of the muscular tissue corresponding to it. In general arrangement it closely resembles what is seen in tendon. The contractile material of muscle may be shown to be continuous with the germinal matter, and oftentimes a thin filament of the transversely striated tissue may be detached with the oval mass of germinal matter still connected with it, showing that, as in tendon, the germinal matter passes uninterruptedly into

the formed material. In the formation of the contractile tissue, the germinal matter seems to move onwards, while posteriorly, it gradually undergoes conversion into tissue. At the same time it absorbs nutrient material, and thus there may be no loss in bulk in a mass which has been instrumental in the production of a considerable amount of contractile tissue.

The drawings represented in fig. 41, plate IV, will enable the student to understand the relation of the germinal matter to the contractile tissue, or formed material of muscle.

On the Formation of Nerve Fibres.—Nerve fibres consist of formed material which is structurally continuous with that of the cells with which they are connected. At an early period of its development a nerve fibre appears to consist of a number of masses of germinal matter, linearly arranged. As development advances, these become separated further and further from one another, and the tissue formed between them constitutes the fibre of the nerve. Fig 42, plate IV, represents a dark-bordered nerve fibre from the frog at an early period of its development.

Of Living or Germinal Matter. Of the "Nucleus" and "Nucleolus."—In the foregoing account of the structure and mode of formation of tissue it has been shown that even the smallest living organism with which we are acquainted does not consist of matter in the same state in every part, but that the material within (germinal or living matter) possesses powers or properties of which the formed material, be it solid or fluid, is entirely destitute. Each mass of germinal matter with a proportion of the formed material around it, is a cell. All living cells consist of matter in these two very different states. The one state being an active condition *vital;* the other being a passive state in which no *vital* actions are manifested.

The importance of this distinction is very great, because, as will presently be shown, the matter in the first or living state is that upon which all growth, multiplication, conversion, formation, in short *life*, depends; while, in the second condition, the matter may exhibit very peculiar properties, and it may have a most complex chemical composition; but although it may increase by new matter being *added to it*, it does not grow or multiply, it does not convert or form—it does not

live. Lastly, facts and arguments have been advanced which show that all matter in the last or formed state was once in the first or living state, so that the properties it has acquired, and the characters it possesses as formed matter, depend upon the changes which were brought about while the matter existed in the germinal or living state.

One mass of living germinal matter may divide into several, and thus cell-multiplication occurs. In all cases the multiplication of the cell is due not to a *growing in* of the wall or formed material, but entirely to changes in the germinal matter.

In many masses of germinal matter a smaller spherical mass, often appearing a mere point, is observed, and in many cases this divides before the division of the parent mass takes place. This, however, is not necessary to the process, for it takes place in cases in which no such bodies are to be seen, and it frequently happens that one or more of these smaller spots or spherical masses may appear in its substance, *after* a portion of germinal matter has been detached from the parent mass. These are to be regarded as new centres composed of living matter. Within these a second series is sometimes produced. The first have been called *nuclei*, and those within them *nucleoli*. Marvellous powers have been attributed to nuclei and nucleoli, and by many they are supposed to be the agents alone concerned in the process of multiplication and reproduction. These nuclei and nucleoli are always more intensely coloured with alkaline colouring matters than other parts of the living or germinal matter, a fact which is alone sufficient to show the difference between a true nucleolus or new centre and an oil globule, which has often been wrongly termed a nucleolus. According to the view of cell-structure here advanced, nuclei and nucleoli are but new living centres appearing in pre-existing centres, and they may be supposed to mark the commencement of another series of changes in the matter in which they appeared, differing, perhaps, in some minor particulars from the first changes which occurred. Sometimes a very defined line shows precisely the limit of the two orders of changes. Although nuclei and nucleoli are germinal or living matter, both are not undergoing conversion into formed material. The vital powers of nuclei are often not manifested at all, but under certain conditions the nucleus may increase, and exhibit all the phenomena of ordinary

[illegible]ERMINAL OR LIVING, AND FORMED MATTE[illegible] OF THE CELL.

Fig. 37.

[illegible] Showing germinal matter and formed material (inter-cellular substance of authors), with [illegible] resembling a cell wall. × 700. p 85

Fig. 38.

Tendon. Kitten at birth. × 215. p 86.

Fig. 39.

Tendon. Young cat. × 215. p 86

Showing germinal matter and formed material (inter-cellular substance, of authors) of tendon at different stages of development.

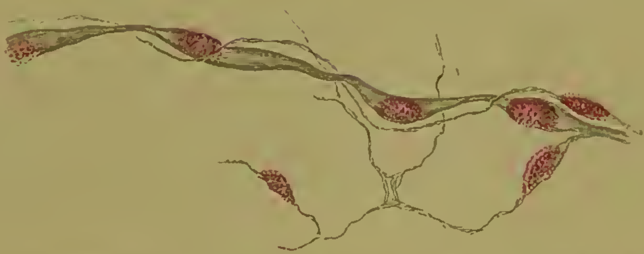
Fig. 40.

[illegible] with straight [illegible] al fibres. Frog. p 84

Fig. 41.

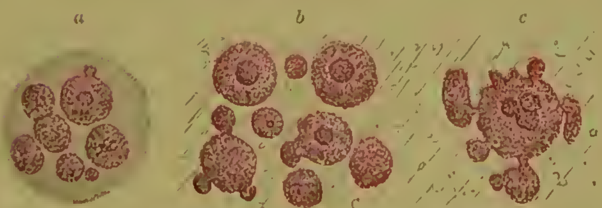
Muscle. Germinal matter and formed material. *a*, the sarcolemma. *b*, the contractile material. The arrows show the direction in which the masses of germinal matter are supposed to be moving. p 87

Fig. 42.



[illegible] Bladder of frog. Showing germinal matter and formed material of nerve cells or elementary parts. × about 1800. p 87

Fig. 43.



[illegible] or Pus. To illustrate the changes resulting in the germinal matter of an [illegible] cell from increased nutrition, showing the manner in which the germinal [illegible] normal cell, if supplied very freely with pabulum, may give rise to pus. p. [illegible]

(To face p[illegible])

germinal matter—new nuclei may be developed within it, new nucleoli within them so that ordinary germinal matter may become formed material, its nucleus growing larger and taking its place. The original nucleolus now becomes the nucleus, and new nucleoli make their appearance in what was the original nucleolus. The whole process consists of evolution from centres, and the production of new centres within pre-existing centres. Zones of colour, of different intensity, are often observed in a cell coloured with carmine. The outermost or oldest, or that which is losing its vital powers, and becoming converted into formed material, being very slightly coloured, the most central part, or the nucleus, although furthest from the colouring solution, exhibiting the greatest intensity of colour. These points are illustrated in plate III, fig. 36, and some other figures. Germinal matter, in a comparatively quiescent state, is not unfrequently entirely destitute of nuclei, but they sometimes make their appearance if the mass be more freely supplied with nutrient matter. This fact may be noticed in the case of the connective tissue corpuscles, and the masses of germinal matter connected with the walls of vessels, nerves, muscular tissue, epithelium, &c., which often exhibit no nuclei (or according to some, nucleoli), but soon after these bodies become supplied with an increased quantity of pabulum, several small nuclei make their appearance in all parts of the germinal matter.

So far from nuclei being formed first, and the other elements of the cell deposited around them, they make their appearance in the substance of a pre-existing mass of germinal matter, as has been already stated. The true nucleus and nucleolus are not composed of special constituents differing from the germinal matter, nor do they perform any special operation. They consist of living germinal matter. Small oil-globules, which invariably result from post-mortem changes in any germinal matter, have often been mistaken for nuclei and nucleoli.

Of the increase of Cells.—Several distinct modes of cell increase or multiplication have been described, but in all cases the germinal matter divides, and is the only material in the cell actively concerned in the process of multiplication. The process of division may, however, take place according to several different plans :—1. The parent mass of germinal matter may simply divide into two equal parts, apparently in

obedience to a tendency of the portions to move away from one another after the original mass has reached a certain size. During this process, a constricted part is produced between the two separating masses, and this becomes thinner and thinner. This band, reduced to the thinnest line, may still connect the two, or it may break, and thus two independent living masses result from the division of one. 2. The parent mass, instead of dividing into two, may divide into three, four, or more equal parts. 3. From every part of the parent mass, protrusions, buds, or offsets may proceed, and however small these may be, each one, when detached, soon absorbs nutrient matter, and grows until it attains the same size as its parent. The formed material of the cell is perfectly passive in the process of increase and multiplication. If soft or diffluent, a portion of this may collect around each of the masses into which the germinal matter has divided, but it does not '*grow*' or '*move in*' and form a partition as has often been stated. When a septum or partition exists, it results not from "growing in," but it is simply produced by a portion of the germinal matter undergoing conversion into the formed material of which it is composed.

If the formed material of the cell be hard and firm and unyielding, the germinal matter may make its way through some orifice in it, or at the weakest point, and escape in small particles which pass forth into the surrounding medium, or the separating portions may remain attached to the parent for a longer or shorter period of time, in the form of processes or outgrowths, as represented in plate II, fig. 19. In either case its outer part becomes converted into formed material, which protects it and modifies its rate of increase; so that in no case can it be said that the cell, as a whole, divides, but the germinal matter alone is the material which is concerned in this as well as in all other active phenomena characteristic of cell life. If these simple facts be carefully borne in mind, the differences observed in the fully formed textures, and the alterations occurring in disease, receive a ready explanation.

Of Development.—The greater number of living beings result from changes occurring in a minute body of apparently very simple structure, which is formed within the organism of the female parent, and in which active changes commence immediately after its impregnation has taken place. This body is the

ovum or *egg*, which in many cases is provided with a store of nutrient matter, to be appropriated by the embryo during the early period of its development. The essential portion of the ovum is exceedingly minute. It consists of germinal matter which, besides exhibiting special and peculiar characteristics in the course of its development, presents at every period of existence the same general characters, and possesses the same general properties as every other kind of germinal matter. The complete ovum or egg of man and the higher animals exhibits a somewhat complex structure, and certain special parts have received distinct names which it may be well to give. Most externally is the homogeneous *vitelline or yolk membrane*, which contains besides the yolk the essential parts, called the *germinal vesicle*, within which is the *germinal spot*, but these last probably correspond to parts found in the ordinary "cell"—the centre of germinal or living matter, termed the *nucleus*, within which is another centre termed the *nucleolus*. Before an embryo can be developed from the true ovum, impregnation must take place. It is now certain that in this process the male element (including the minute mass of germinal matter it contains?) penetrates quite into the substance of this small mass of living matter, and exerts an influence upon all the phenomena which are to succeed in it. The germinal matter of the ovum having thereby acquired new powers, divides and subdivides, and many series of new masses of germinal matter successively come into existence, disappear, and give place to new ones, each series being however the descendant of that which existed before, until at last a number of masses result, from which the earliest traces of the new being or embryo are evolved. But there are many instances of beings of comparatively simple organisation from which a new organism may result without the formation of a true ovum. Certain masses, and, in some cases, every mass of germinal matter in the body, may give rise to the formation of new and complete organisms. To this process there is some analogy even in the highest animals, and at all periods of life, in the development of simple masses of living matter into new tissues of very complex structure.

We are quite unable to offer any clear and satisfactory explanation of the phenomena of development of a tissue or

organ. It has been shown that the successive generations of cells produced are lineal descendants of the original cell or cells constituting the germ-cell, while the arrangement, structure, and composition of the elementary tissue formed, differ materially as the development of the texture or organ advances. The successive production of formed material differing in composition and properties from that previously produced may be accounted for upon the supposition that the successive series of masses of germinal matter possess different powers, but whether this power is acquired during the process of their development or transmitted directly from the original germinal matter we have at present no positive evidence to show. That the new living centres which are developed within pre-existing living masses of germinal matter exhibit powers or properties not possessed by those within which they originated is certain, and it is probable that this origin of new centres within pre-existing ones takes place in all cases, and is an essential phenomenon in development. It is interesting to observe, that a mass of germinal matter which remains *quiescent* for a certain period of time and absorbs scarcely any pabulum, or perhaps actually none, may give origin to descendants from which special and complex structures and organs not previously formed may be produced; while if this very same mass were to be too freely supplied with pabulum, it would grow and multiply, and would exhibit the greatest activity, but not one of its very numerous descendants would be capable of giving rise to any structure. After existing for a very brief period they would die without leaving any evidence of their having possessed any structure-forming power whatever. Increase in power seems to be associated with the most limited change in germinal matter, while rapid change—increased vital action—seems to be invariably connected with decadence in power. So that the formation of highly elaborate and complex tissues, organs, or organisms, is not in any way connected with, or due to the influence of, the ordinary forces associated with lifeless matter, but it must be attributed to the influence of some peculiar power capable of controlling and directing both matter and force, and therefore of a nature very different to ordinary force. The laws governing vital phenomena are not yet understood. It will naturally be suggested that the different substances and

different structures produced by germinal matter at different periods of development may depend upon the different surrounding conditions present when the changes occur. This, however, is no explanation at all, for the surrounding conditions present, as well as the circumstances concerned in their production, are themselves complex. They are not simple external conditions, but are in part the result of external circumstances, and in part of a previous state of things in the establishment of which pre-existing vital powers associated with germinal matter played no unimportant part. Extending our inquiries still further back, we must at length discuss how the first formed material itself was produced, and it has been shown that this is due to the death of living matter under certain conditions, which is itself a highly complex phenomenon, and cannot be explained without supposing certain *internal* forces capable of causing the elements of the matter to arrange themselves in a certain definite manner, totally different to that in which the ordinary forces of matter would cause these elements to be arranged,—and certain *influences operating from without* (surrounding external conditions) tending to prevent the supposed internal forces from exerting their sway. The composition, structure, and properties of the matter produced must, in fact, be referred to the influence of very different and antagonistic forces acting upon matter from opposite directions.

Of the Changes in the Cell in Disease.—It has been shown that of the different constituents of the fully formed cell, the germinal matter is alone concerned in all active change. This is in fact the only portion of the cell which lives, while at an early period of development, the parts of the cell usually regarded as necessary to cell existence are altogether absent. The "cell" at this period is but a mass of living germinal matter, and in certain parts of the body at all periods of life are masses of germinal matter, destitute of any cell-wall, and exactly resembling those of which at an early period the embryo is entirely composed. White blood and lymph corpuscles, chyle corpuscles, many of the corpuscles in the spleen, thymus and thyroid, corpuscles in the solitary glands, in the villi, some of those upon the surface of mucous membranes, and minute corpuscles in many other localities, consist of living germinal matter. There is no structure through which these soft living

particles may not make their way. The destruction of tissue may be very quickly effected by them, and there is no operation peculiar to living beings in which germinal or living matter does not take part. Any sketch of the structure of the cell would be incomplete without an account of some of the essential alterations which take place in disease, and it is therefore proposed to refer very briefly to the general nature of some of the most important morbid changes.

If the conditions under which cells ordinarily live be modified beyond a certain limit, a *morbid* change may result. For instance, if cells, which in their normal state grow slowly, be supplied with an excess of nutrient pabulum, and increase in number very quickly, a *morbid* state is produced. Or if, on the other hand, the rate at which multiplication takes place be reduced in consequence of an insufficient supply of nourishment, or from other causes, a diseased state may result. So that, in the great majority of cases, disease, or the morbid state, essentially differs from health, or the healthy state, in an increased or reduced rate of growth and multiplication of the germinal matter of a particular tissue or organ. In the process of inflammation, in the formation of inflammatory products, as lymph and pus, in the production of tubercle, and cancer, we see the results of increased multiplication of the germinal matter of the tissues or of that derived from the blood. In the shrinking, and hardening, and wasting, which occur in many tissues and organs in disease, we see the effects of the germinal matter of a texture being supplied with too little nutrient pabulum, in consequence sometimes of an alteration in the pabulum itself, sometimes of an undue thickening and condensation of the tissue which forms the permeable septum, intervening between the pabulum and the germinal matter.

The above observations may be illustrated by reference to what takes place when pus is formed from an epithelial cell, in which the nutrition of the germinal matter, and consequently its rate of growth, is much increased. And the changes which occur in the liver cell in cases of cirrhosis may be advanced in illustration of a disease which consists essentially in the occurrence of changes more slowly than in the normal condition, consequent upon less than the normal freedom of access of pabulum to the germinal matter.

The outer hardened formed material of an epithelial cell may be torn or ruptured mechanically, as in a scratch or prick by insects, or it may be rendered soft and more permeable to nutrient pabulum by the action of certain fluids which bathe it. In either case it is clear that *the access of pabulum to the germinal matter is facilitated*, and the latter necessarily "*grows*"—that is, converts certain of the constituents of the pabulum that come into contact with it into matter like itself,—at an increased rate. The mass of germinal matter increases in size and soon begins to divide into smaller portions. Parts seem to move away from the general mass. These at length become detached, and thus several separate masses of germinal matter, which are embedded in the softened and altered formed material, result. These changes will be understood by reference to fig. 43, *a*, *b*, *c*, plate IV. In this way the so-called inflammatory product *pus* results. The abnormal pus-corpuscle may be produced from the *germinal or living matter of a normal epithelial cell, the germinal matter of which has been supplied with pabulum much more freely than in the normal state.*

It will be seen how easily the nature of the changes occurring in cells in inflammation can be explained if the artificial nomenclature of cell-wall, cell-contents, nucleus, be given up. In all acute internal inflammations a much larger quantity of inanimate pabulum is taken up by certain cells and converted into living matter than in the normal state. Hence there is increase in bulk. Cells of particular organs, which live very slowly in health, live very fast in certain forms of disease. More pabulum reaches them, and they grow more rapidly in consequence.

In cells which have been growing very rapidly and are returning to their normal condition, *in which the access of nutrient pabulum is more restricted than in the abnormal state*, as is the case in normal cells passing from the embryonic to the fully-formed state, the outer part of the germinal matter undergoes conversion into formed material, and this last increases as the supply of pabulum becomes reduced.

We will now enquire what alterations can be observed in cells, the "*formed material*" of which, under *normal conditions*, becomes *quickly* resolved into other soluble constituents if these cells be placed under circumstances which caused the formed

material to become harder and less permeable to nutrient matter than in health. The formed material which enters into the formation of the liver "cell" is soft, moist, and readily permeable to certain nutrient matters. There is no cell-wall, but the outer part of the formed material is gradually resolved into soluble biliary matters, which pass down the ducts, and into amyloid and saccharine matters, which permeate the walls of the vessels and enter the blood. To make up for the disintegration of the outer part of the formed material, new formed material is produced in the interior of the cell from the germinal matter, and the germinal matter which undergoes this change is replaced by new germinal matter produced from the pabulum that is absorbed. If such cells and their descendants are bathed with improper pabulum, and especially with substances which render albuminous matters insoluble, or possess the property of hardening them, they necessarily diminish in size, in consequence of the formed material becoming less permeable, less nutrient matter is taken up; and of course, as the formed material becomes hardened, less disintegration takes place, the quantity of secretion, which really consists of the products resulting from disintegration, is much diminished, and the amount of work performed by the cell is reduced. Under the supposed conditions the cells shrink in size and become more firm in texture. Many gradually waste, and not a few die, and at length disappear. These seem to be the essential changes which slowly take place in the liver cells in *Cirrhosis*, and to these changes in the cells, the striking shrinking and condensation of the whole liver, so characteristic of this disease are due.

From these observations it follows that disease may result in two ways—either from the cells of an organ growing and multiplying faster than in the normal state, or more slowly. In the one case, *the normal restrictions under which growth takes place are diminished; in the other, the restrictions are greatly increased. Pneumonia*, or inflammation of the lung, may be adduced as a striking example of the first condition, for in this disease millions of cells are very rapidly produced in the air cells of the lung, and nutrient constituents are diverted from other parts of the body to this focus of morbid activity. Contraction and condensation of the liver, kidney, and other glands, hardening, shrinking, and wasting the muscular, nervous, and other

tissues, are good examples of the second. The amount of change becomes less and less as the morbid state advances, the whole organ wastes, and the secreting structure shrinks, and at last inactive connective tissue alone marks the seat where most active and energetic changes once occurred. It is easy to see how such a substance as alcohol must tend to restrict the rapid multiplication of the cells if the process is too active, and how it would tend to promote the advance of disease in organs in which rapid change in the cells characterises the normal state.

We shall necessarily be led by these considerations to the conclusion that the rate of growth of cells in disease may be accelerated or retarded by an alteration in the character of the pabulum which is transmitted to them, and we shall be led to search for remedies which have the property of rendering tissues more or less permeable to nutrient fluids, or which alter the character of the fluid itself. Such considerations are of interest not to the physiologist only, but they have a very important bearing upon the practical treatment of disease.

It has been sought in this chapter to establish the fact that all formed matter results from changes in the germinal matter, and that the action of the cell consists really in a change from the living to the lifeless state of the matter of which it is composed. This change takes place in the same definite direction in all cases. The changes in the germinal or living matter must be attributed to the influence of a supposed vital force or power by which the matter is temporarily affected. The products formed by the cell do not depend upon any metabolic action exerted by the cell-wall or nucleus upon pabulum, nor are they simply separated from, or deposited by, the blood. The matter has passed through the living state, and by ceasing to live under certain conditions, the lifeless formed materials in question have resulted. The view here advanced leads us to look upon the 'living cell' as a minute body, consisting partly of living matter influenced by vital force, partly of lifeless matter resulting from the death of the first, in which chemical and physical changes occur, and these may be modified by the influence of surrounding substances and external forces.

CHAPTER II.

OF COMPOSITION.—CHEMICAL COMPOSITION OF GERMINAL MATTER AND FORMED MATERIAL.—SKETCH OF THE CHEMICAL CHANGES OCCURRING IN THE SIMPLE LIVING CELL.—CHEMICAL CHANGES IN THE ORGANISM AT DIFFERENT PERIODS OF DEVELOPMENT.—OF THE BLOOD.—OF THE CHANGES RESULTING FROM OXIDATION.—OF THE FORMATION OF VARIOUS COMPOUNDS IN DIFFERENT TISSUES AND ORGANS OF THE BODY.—THE CONVERSION OF PABULUM INTO BLOOD.

ANIMAL bodies are composed of solids, liquids, and gases, the last being held in solution in the liquids.

Solids and Liquids.—The solid textures contain only about one-fourth of solid matter, the rest is water. The great shrinking which they experience when dried, shows how much of their bulk they owe to this combination; and parts thus shrunken swell out again, and assume their natural condition on the addition of water. Nor does this swelling out after shrinking occur in water alone. The most soft and delicate tissues will regain their former volume, even if placed in very viscid fluids as syrup or glycerin, of much higher specific gravity than the tissues immersed. This seems to be due to the inherent elastic property in the tissue itself, in virtue of which its anatomical elements tend to assume the position and form they originally held in the natural state of the texture. The quantity of water existing, even in the hardest tissues, is far greater than would be supposed. The mummy of a large man is of very trifling weight. Blumenbach possessed the entire *perfectly dry* mummy of a Guanche, or aboriginal inhabitant of Teneriffe, presented to him by Sir Joseph Banks, which, with all its muscles and viscera, weighed only seven pounds and a half.

Water is one of the most important constituents of animal bodies. It forms four-fifths of their nutrient fluid, the blood; and it gives more or less of flexibility and softness to the various solid textures. The loss of it in great quantity speedily puts a stop to *vital*, as well as chemical and physical, action. Germinal matter is itself semi-fluid, and the very active move-

ments of the portions of which it consists, which seem essential to the living state of matter, could not take place unless every portion of a living mass were free to move in fluid, or contained so much fluid as to be readily moveable, not only around, but through other portions. Water is a solvent of many organic and inorganic matters; it is, therefore, a valuable medium for conveying these substances to and from the several textures and organs. Moreover, it dissolves various gases. Oxygen is thus carried in solution to various parts of the body, where it acts upon certain of the insoluble solids, which are thereby oxidized and rendered soluble. The substances thus formed are carried away in solution. Water plays a most important part in the various chemical operations of the body; and by its addition to or subtraction from a particular compound, an alteration in its properties may be induced.

The various methods at our disposal for separating from one another the different compounds formed by living beings, and of resolving these into their ultimate elements, belong respectively to the departments of *proximate* and *ultimate analysis.* (See page 5.)

Organic and Inorganic Matters.—The solid textures and the soluble substances held in solution in the fluids of the body, consist of two classes of compounds, spoken of as *organic* and *inorganic.* But many of the so-called organic substances have been prepared artificially in the laboratory, and they cannot therefore be considered as peculiar to living beings. The organic matters are decomposed by a red heat, while the inorganic or mineral substances are not destroyed by incineration.

Organic compounds are composed of certain of the non-metallic elements, and principally of oxygen, hydrogen, nitrogen, and carbon. These elements, in the living body, are combined so as to form complex but often unstable compounds, and, under certain conditions, by hydration or by the appropriation of oxygen and other substances, these organic compounds may be afterwards split up, as it were, into much simpler but more stable bodies.

The organic compounds which enter so largely into the composition of the various solids and liquids of living beings, differ from one another, in composition and properties, in the

most remarkable manner. Many have been placed by chemists in certain artificial groups, but hitherto it has not been found possible to arrange more than a very few in a naturally connected chemical series. The corresponding substances in different animals exhibit differences of properties and composition; and in disease, the characters and composition of the chemical components of the tissues and fluids undergo remarkable variations. Nor has any definite relation been proved to exist between the chemical composition, form, structure, and properties of organic, any more than inorganic bodies.

Of the different Constitution of the Corresponding Substances in different Animals.—There are many modified forms of albumen, fibrin, and casein, several different varieties of starch, sugar, fat, &c., numerous different forms of hæmato-crystallin, biliary acids, &c., and the difference is not explained by the varying conditions under which these substances have been produced, but must be ascribed partly to these and partly to the different properties and powers of the germinal or living matter taking part in their production. We have already observed that the tissues which precisely correspond to one another in different animals exhibit minute, but still very appreciable, differences in their *structure*, and we should, therefore, be led to anticipate that differences in the arrangement of their elements, and in their chemical properties, would also exist. Nor are these differences in chemical constitution confined to allied organic compounds, they are found to obtain also in the case of many inorganic salts.

Chemical Substances composing the Tissues, not found in the Blood. The chemical compounds entering into the formation of the solid tissues and liquid secretions have not for the most part been detected in the blood or nutrient pabulum, and there is reason to think that they have resulted, not from chemical changes taking place while the solutions traversed vessels or permeated membranes, but that they are the consequence of changes occurring in the temporary or living state, through which, as has been already shown, the various elements of the food must pass before they form a constituent part of the tissues or nutrient fluids of living beings. The germinal or living matter is alone concerned in this process, and different kinds of germinal matter, although, as far as we can tell, having the same com-

position, and certainly nourished by the same pabulum, may give rise to the formation of very different compounds. It may, indeed, be regarded as certain, that from a nutrient fluid common to them all, the masses of germinal matter of different textures take certain constituents which become converted into the tissues, or the constituents peculiar to the different secretions. The idea that these very substances existed in a modified form in the blood, and were merely *separated* from it by a sort of attractive force existing in the cells, will probably soon give place to the doctrine now supported by so many facts, that, from the same chemical constituents, different kinds of living matter may prepare or produce compounds very different in composition and properties from one another. For the crude notion that the formation of tissues was akin to the process of crystallisation, we must substitute the conclusion that the real cause of the peculiar composition and properties of the substances formed, is to be sought for in the living matter itself. And as the evidence that the wonderful changes occurring in this matter are due to the influence of some peculiar force or power, becomes stronger, it is to be hoped that comparisons between living things, and crystals laboratories or steam-engines, will no longer be insisted upon.

OF THE CHEMICAL CHANGES OCCURRING IN THE CELL.

Before we can hope to form a correct idea of the complex chemical phenomena occurring in man and the higher animals at any period of existence, we must have a knowledge of the general chemical changes occurring in the cell. Regarding the "cell" as consisting of—1. Germinal or living matter. 2. Formed matter; and 3. Formed matter undergoing disintegration, the consideration of the chemistry of the cell naturally falls under three heads;—*The Chemistry of the germinal matter*, *the Chemistry of the formed material, and the Chemistry of the substances resulting from the oxidation of, or other changes in the formed material.* This will, therefore, be discussed in the first place, and then we shall have to consider the more complex chemical phenomena occurring in man and the higher animals at different periods of existence.

The Chemical Characters of the Living Germinal Matter.—Just as the various tissues of living beings result from changes

occurring in a perfectly transparent, structureless, germinal or *living* matter, so the numerous chemical compounds characteristic of different living organisms, and different tissues and organs, result from changes taking place in this same transparent material. Few substances which enter the organism of a living being pass through unchanged, without having their elements completely rearranged. There is reason to believe, that even the elements of many mineral substances become separated from one another, and recombined in the body.

It is remarkable that the germinal matter from the most dissimilar living beings presents the same characters, so that it is not possible to premise, from any microscopical or chemical examination, what will be the nature of the substances formed from any given mass of germinal matter. The general characters of germinal matter have been already referred to, and the student will readily form a notion of its simple transparent, jelly-like appearance, if he examines, under a high magnifying power, a white blood corpuscle, or the transparent moving matter forming the substance (sarcode) of a common *amœba*, specimens of which can always be obtained from water, in which a little dead animal tissue has been placed, left to stand for some days in a light part of the room.

There is no living or germinal matter which does not contain oxygen, hydrogen, nitrogen and carbon; and although some of the other elements are often present and are, undoubtedly, of great importance in special cases, the above are constantly found and seem essential to the very existence of vital changes. It is comparatively easy to ascertain what elements exist in the living matter, but it is not possible to demonstrate how these are combined, or if they are combined at all. Of the relation which these elements bear to one another in the living matter, we know indeed nothing; but since every kind of living matter exhibits the same characters, it seems probable that during this temporary living state, the elements do not exist in a state of ordinary chemical combination at all. Their ordinary attractions or affinities seem to be suspended for the time. That the matter is in a state of active molecular change, or vibration, is certain, but it is doubtful if chemical combination is possible as long as the matter *lives*. No chemical compound or elementary substance,

as far as is yet known, exhibits life, or posesses vital properties or endowments. It is perhaps as impossible to conceive a *living chemical compound* as it is to conceive a *living elementary atom.* And the chemist who supposes that he can analyse *living* matter is in error, for he examines not the matter which is alive, but simply lifeless compounds resulting from its death. When the living or germinal matter is converted into formed matter, combination of its elements takes place, free oxygen being in some cases absorbed at the moment, and compounds of such complex nature result that the efforts of chemists to ascertain the chemical relations or the exact composition of many of them have not hitherto met with success. And it often happens that the chemical compound undergoes further change after it has been formed, so that the substance which we submit to examination in our laboratories, is not of the same chemical composition as when it was first produced by the cell.

Of the Production of Chemical Compounds (formed material) from Germinal Matter.—It is remarkable that the elements of every kind of germinal matter, when its life is *suddenly* destroyed, should combine to form compounds closely allied to one another in chemical composition and properties, and that an *acid* reaction should be always developed. From every kind of germinal matter a material which *coagulates spontaneously*, and one which is *coagulated by heat and nitric acid* may be obtained. The first of these is *fibrin*, and the second is *albumen.* Fibrin, albumen, water and certain salts, may be obtained from every kind of germinal matter. All kinds of germinal matter also yield fatty matters, and these continue to increase in quantity for some time after death has occurred. As is well known, the "nuclei" (germinal matter) of all organisms and tissues which have been kept for some time in preservative fluids become granular, and usually distinct globules are to be seen. These granules and globules are due to the formation of fatty matter from the germinal matter itself, or from the albumen, fibrin, and other substances immediately resulting from its death. It is very remarkable that the general characters, if not the chemical composition, of this fatty matter, should be the same in the case of every kind of germinal matter in both vegetable and animal tissues (see page 110). It would appear that the elements of every kind of germinal matter are so disposed or

arranged during the living state, that they may combine to form water, albuminous matters including fibrin, fatty matters, and salts.

Although water may be obtained from every kind of living matter it is doubtful if water in its ordinary condition exists while the matter is alive, for this living matter may be exposed to a temperature considerably below the freezing point of water without becoming solid, and it is probable that death must occur before the actual congelation of the germinal matter, or of the water it contains, can take place.

The formation of all chemical compounds seems to be connected with the *death* of the germinal matter, and different substances will result according as the death is sudden or gradual, that is, according as the germinal matter dies suddenly *en masse* or more slowly, particle by particle. And it is probable that in the comparatively slow molecular death, a certain amount of oxygen is taken up at the moment of combination, and this alone would give rise to very different combinations to those which occur when the living matter is suddenly destroyed, little or no oxygen being present. An alteration in the conditions under which death takes place will be associated with a difference in composition of the materials produced; but it must not be supposed that external conditions alone determine either the form, composition or properties of the resulting substances.

When germinal matter becomes resolved into formed material, other compounds are produced besides the special ones which characterise that particular kind of germinal matter; and a product which largely predominates under certain circumstances may be produced in mere traces under other conditions. For instance, the germinal matter of the liver cell of some animals becomes resolved into amyloid matters and biliary matters with mere traces of fat. In others, fat which accumulates seems to form the main portion of the formed material produced. In man, under some circumstances, bile and amyloid appear to be produced; under others, fat seems to be the main product as in the fish. And various secondary morbid changes are brought about according as the formation of fatty, amyloid or saccharine matter predominates. The nature of the pabulum doubtless affects the composition of the formed materials

produced by the cell, but this is only one of the many circumstances influencing the result. The products resulting from the changes of germinal matter seem to be almost infinitely varied, and those substances which exactly correspond in different animals do not exhibit the same composition. Even in the case of animals very closely allied zoologically, great differences are noticed. The bile, blood, milk, fat, &c., exhibit great difference in composition, although they possess many characters in common, and perform the same offices in the different animals respectively. There appears to be a resemblance generically, associated with striking specific differences.

The germinal or living matter of all living beings, vegetable as well as animal, contains nitrogen, and the broad difference between the changes in the animal and vegetable kingdoms seems to be that in the first a large proportion of the nitrogen entering into the composition of the germinal matter, enters into combination with other elements in the resulting formed substance; while in the latter, as a rule, the nitrogen although necessary to the germinal matter, does not enter into combination, so that while the animal requires a large quantity of nitrogen in its food to supply that which has been converted into various chemical compounds formed by the germinal matter, the plant needs but a very small proportion, because so little enters into the composition of the formed material produced. The tissues of fungi, however, contain a considerable proportion of nitrogen.

Certain saline or inorganic substances form constant and very important constituents of the animal body. Although it is possible that vital changes may continue to go on in the absence of saline substances, it is certain that the tissues, upon the integrity of which the duration of life depends, could not be produced or nourished without them. *Chloride of sodium* is one of the most important. This salt is always present in large proportion in all embryonic tissues, and it is probable that it is intimately concerned in some of the active changes taking place in the germinal matter itself. Whenever germinal matter is growing and multiplying very rapidly in the human organism, chloride of sodium is present, and it is probable that in the lower organisms and plants, other saline substances are of equal importance in corresponding processes.

Of the Chemical Changes taking place in the Formed Material after its production.—Most important alterations may occur in the formed material after it has been produced. In some cases it undergoes condensation, during which process structural peculiarities manifest themselves. Gradually, the formed material may become dry, after which, little alteration takes place. But in the soft, moist formed material, produced by many of the cells in the internal organs of the body, the most important changes occur. In some cases the formed material is perfectly fluid, and splits up into soluble or gaseous substances as soon as it is produced. In many instances, the elements of the formed material, although themselves insoluble, gradually undergo conversion into soluble compounds, in consequence of the action of oxygen, which combines with certain of the elements. If, in any case, the supply of oxygen be insufficient to convert the whole of the matter present into fully oxidised and completely soluble compounds, its elements may combine to form less soluble substances, which accumulate, and in many tissues give rise to morbid change. Hence it is of the utmost importance that the disintegrating processes in the internal organs of the higher animals should be in a state of due activity, for unless the formed material be constantly traversed by fluids rich in oxygen, the products necessarily resulting from disintegration are not fully oxidised and quickly removed in a very soluble form, but remain in the tissue in other states of combination, interfering with its function or even causing suspension of its action altogether. For instance, by the imperfect oxidation of the elements resulting from the disintegration of muscular and other tissues, fatty matters result, and if the conditions giving rise to their production continue, these accumulate, leading to various morbid conditions. Insufficient oxidation seems to be the main cause of the accumulation of uric acid, oxalates and fatty matters in the blood. Leucine, tyrosine, sugar and many other substances result from the ordinary chemical changes being interfered with. Their formation is perhaps due to the existence of conditions which interfere with the combination of the due proportion of oxygen with the elements of the compounds which unites with them under ordinary circumstances.

Sketch of the Chemical Changes occurring in the simple Cell.—Carrying out our inquiry according to the plan adopted in the chapter devoted to the consideration of structure, we may now consider the chemical changes which occur during the life of a simple cell, and we propose to select, for the purposes of inquiry, one of the lower microscopic fungi—the yeast plant.

If a minute germ of this vegetable organism be placed in a solution containing a trace of albuminous matter, a small quantity of phosphatic salts, and sugar in the proportion of about 4 parts of sugar to 20 of water, and the whole be exposed to the air, at a temperature of about 80°, growth will take place. The germ will give rise, in a short time, to many bodies like itself, and the sugar will be gradually appropriated by the plant, which will increase in size, divide and subdivide, until the greater part of the sugar has been removed. Now, in this process, as the sugar disappears, and the yeast corpuscles multiply, while oxygen and albuminous matter are taken up, carbonic acid and alcohol are evolved in considerable quantity. This is the process known as *alcoholic fermentation*, and there is no doubt that the formation of the alcohol and carbonic acid is intimately connected with the growth and multiplication of the yeast cells, but the precise manner in which the decomposition of the sugar is effected is still unknown. Many chemists, following Liebig, probably regard the change as too purely chemical. Because putrefying blood, white of egg, &c., caused the fermentation of sugar, Liebig came to the conclusion that yeast was a sort of vegetable fibrin, albumen, or caseine in a state of decomposition. We now know that putrefying substances themselves cause fermentation, only because they contain living organisms. It was supposed that the yeast cells effected the decomposition of the sugar without necessarily coming into actual contact with every portion of sugar, by virtue of some action, the nature of which was not explained, but which was spoken of as metabolic action. Mitscherlich proved, however, that for the change to occur, the living cells of the yeast plant must come into actual contact with every particle of syrup to be decomposed.

We may now consider this question from a somewhat different point of view. The germinal matter of yeast, like other kinds of germinal matter, contains nitrogen and exhibits

an acid reaction. An albuminous substance may be obtained from it, as well as from all other kinds of germinal matter. The formed material of yeast—the envelope or cell-wall produced from the germinal matter (see page 77), consists, according to Mülder, of a substance closely allied to cellulose in composition. It is, then, a fact, that by the growth and multiplication of the germinal matter of the yeast cell, cellulose, carbonic acid, alcohol, a little lactic acid, and some other substances of less importance result; but the precise manner in which all these substances are produced, has not been determined. From what has been already stated, in chapter 1, it would appear probable that the nutrition and growth of the yeast plant occur somewhat as follows:—the cell takes up a certain quantity of sugar, with a trace of albuminous matter salts and perhaps oxygen, and these undergo conversion into germinal matter. At the same time the germinal matter already produced upon the surface undergoes conversion into formed material (see page 77), and this formed matter immediately becomes resolved into *cellulose*, which is precipitated, and *carbonic acid* and *alcohol*, which are soluble. All these substances probably result from the death of the germinal matter of yeast. The cellulose forms the insoluble capsule, envelope, or cell-wall, which is permeable to fluids in both directions. The carbonic acid and alcohol being soluble, pass into the surrounding water, and at length escape. Under certain conditions, the proportion of carbonic acid and alcohol formed is great, and the amount of cellulose small, while other conditions seem more favourable to the production of cellulose matter.

The germinal matter of some vegetable cells gives rise to cellulose upon the surface, while within starchy matter is deposited. In other cases chlorophyl and other colouring matters result from changes occurring in the germinal matter (primordial utricle) in the interior of the cell, after the formation of the cellulose wall upon its surface. In all these cases the formation of the peculiar and characteristic substance which accumulates, is accompanied by the formation of soluble and gaseous matters which escape. The germinal matter of the cells of the leaves and flowers of plants becomes resolved into peculiar coloured compounds, and these are often diffused through the germinal matter, but sometimes collect upon its

surface. The germinal matter itself is never coloured, for the soluble coloured matter may be separated from the colourless germinal matter. The formation of chlorophyl from germinal matter may be studied in many of the lower plants, and its separation from the germinal matter effected. In like manner coloured matter may be separated from the colourless germinal matter of many of the young red blood corpuscles of mammalian animals which consist principally of germinal matter.

It is probable that in animal cells also, the formation of several chemical compounds from the germinal matter at the same moment occurs. In the liver cell, for instance, four distinct classes of solid matters seem to be produced by the re-arrangement of the elements of the germinal matter—resinous biliary acids, fatty matter, albuminous matter and amyloid substance. The relative proportion of these different substances produced seems to vary according to different circumstances. Sometimes the quantity of fatty matter is enormous, while in other instances only a mere trace is produced, and the same remark applies to the other constituents.

If, according to the view generally entertained, the different substances entering into the composition of a complex secretion, are separated from the blood and afterwards altered in composition by some unexplained action of the cell, or its nucleus, how are we to account for the fact of distinct classes of substances being separated, or separated and altered, by the agency of one and the same cell or nucleus? The oily, saccharine, and albuminous constituents (butter, sugar, caseine) of milk, have not been discovered in the blood, and there is only one kind of cell to form these three classes of substances. Does the same cell-wall or nucleus separate from the blood at the same time oily, starchy or saccharine, and albuminous matters, and convert these into the particular constituents of milk, or are they separated one after the other? Upon either supposition it would be extremely difficult to account for the actual facts, while, if, as has been rendered probable by different arguments already advanced, the constituents, absorbed from the blood, become first converted into germinal matter, which at length becomes resolved into these three classes of substances, at least a more plausible theory, if not a complete explanation, of the process, is arrived at.

The study of the circumstances under which these different classes of substances are produced by a single cell, and more especially the careful investigation of the conditions which determine a variation in the relative proportion of the different constituents, will greatly contribute to advance our knowledge of many of the most important morbid conditions, and thus give to practical medicine a stronger title to be considered a science.

OF THE CHEMICAL CHANGES OCCURRING IN THE ORGANISM AT DIFFERENT PERIODS OF DEVELOPMENT.

Although we are quite unable to give even a very imperfect idea of the chemical phenomena occurring in man at different periods of his development, we shall make the attempt to employ the imperfect data we possess, and consider some of the most important chemical changes occurring in the organism from the point of view already indicated.

At the earliest period of its development, the simple mass or collection of masses of germinal matter of which the embryo is composed, exhibits a chemistry simple as compared with that of the organism when its development is more advanced. The formed material resulting from the germinal matter, seems to consist principally of albuminous and fatty materials, without any substance capable of yielding gelatin. Saline matters may be detected, and it is certain that amyloid matter soon makes its appearance among the chemical substances produced in the embryo. The *albuminous matter* is closely allied to ordinary albumen, and with it is associated a small quantity of a coagulable matter, probably identical with fibrin.

Fatty Matter.—Little is known concerning the actual chemical nature of the fatty matter developed at the earliest periods of embryonic life, but the compound substance known as myelin, makes its appearance very early. The oil globules so commonly seen in germinal matter of various kinds, especially at an early period of development, and which have been sometimes termed nucleoli, consist of this form of very peculiar fatty matter. I have already shown that cholesterin, one of its constant constituents, is present in the oil globules found in various cells in fatty degeneration, and more recent examinations, with the aid of the highest powers, have displayed the masses of myelin, exhibiting their characteristic refraction, their

double contours, and twisted forms amongst the germinal matter of pus, cancer, epithelial and other cells (plate VIII, figs. 73, 74), and there can be little doubt from the fact, that Beneke has detected myelin in the young shoots and actively growing buds of the potato, asparagus, and many other plants, that myelin is the particular form of fatty matter which immediately results from changes occurring in germinal matter. The reaction and chemical characters of this substance are described in page 148.

The Saline Constituents consist principally of chlorides, but a small quantity of alkaline and earthy phosphates are also present. The chloride of sodium performs some important office in connection with cell multiplication, as we find this substance invariably present in considerable proportion at an early period of the development of all animal tissues, when the masses of germinal matter are growing and multiplying rapidly. It is possible that salt may be serviceable at the earliest periods of nutritive change, by its property of rendering albumen less viscid, more diffusible, and capable of being very readily appropriated by the growing germinal matter.

Amyloid Substance ($C_6H_{10}O_5$).—As the formed material exhibits firmer consistence and structural peculiarities, a gelatin-yielding substance is produced. But with this is developed much matter of an amyloid or starchy character, sometimes called *glycogen.* This has been particularly studied by Rouget, who detected it in cartilage at an early period of development, and also in fibrous and muscular tissues. The epidermic textures exhibit a considerable proportion, although not a trace can be detected in the same textures in their fully developed state. The same is true of the delicate texture which is at length to become hair, horn, or nail. Dr. McDonnell has shown that this amyloid matter exists in the lung tissue in very large proportion, increasing, as development advances, to nearly twenty per cent., while shortly before birth the quantity is so small that it can scarcely be estimated. It is found in muscular tissue generally, but not in that of the heart, in which, probably from its reaching a state of functional activity long before the muscles of the system generally, the proportion of amyloid is comparatively small. In the liver, the formation of amyloid slowly increases, and after birth, its formation seems almost

restricted to this organ. Throughout life, large quantities of amyloid continue to be produced in the liver, and in certain morbid conditions it accumulates enormously. This production of amyloid is probably associated with rapid change in the germinal matter. If this substance were formed by the germinal matter of the tissues in the adult state, it would exist in such small quantity in proportion to the other matters produced, that we might not be able to detect it by the processes at present at our disposal. With reference to the part played by the amyloid matter in the tissues in early life, it would seem probable, from the researches of Dr. McDonnell, that it appropriates to itself nitrogen, and that in this manner a material is produced which afterwards takes part in tissue formation. The same observer has advanced many arguments in favour of the view, that the amyloid matter, as it slowly escapes from the liver cells in which it was formed, takes to itself nitrogen derived from the retrogressive metamorphosis of fibrin in the blood, and that thus a protein substance, allied to casein and globuline and the matter of which the white blood corpuscles are composed, results.—(*Proceed. Royal Soc.* 1863, vol. xii, p. 478.)

The production of these substances allied to starch and sugar, seems to be associated with limited oxidation. It is probable that the chemical elements which, in the embryo, combine to form starchy matters, would, at a later period of development, combine with oxygen to form carbonic acid and other substances, which would be excreted in a soluble form. This view is confirmed by the fact that, in the liver, in which amyloid matters are being formed throughout life, oxidation is very limited; while those morbid conditions in which the formation of the same substance occurs in connection with many adult tissues, especially the smaller arteries and the nervous tissues, are characterized by a reduction in the activity of this process. Amyloid matter (glycogen) has been detected in the substance of the round worm of the pig (ascaris lumbricoides), by Dr. Michael Forster (*Proceed. Royal Society*, vol. xiv, p. 543, 1865), and it has been found in many of the lower animals, which live under conditions incompatible with a highly active state of the oxidizing processes.

Gelatin-yielding Substance.—The tissues have assumed their permanent anatomical characters, and have commenced to per-

form their normal functions, when the substance which yields gelatin by boiling is produced. At an early period of development, although delicate transparent tissue may be detected, it does not yield gelatin. According to Hoppe, this substance cannot be detected until after the embryo has left the egg. The proportion of the fibrous texture, and gelatin-yielding tissues allied to it, increases as age advances. Gelatin does not exist preformed in the tissues, and can only be obtained by artificial means. If the cutis or true skin, tendon, or bone, be subjected to continued boiling, this substance is obtained in solution in the hot water, and, upon cooling, assumes the form of a solid jelly, which is the more solid as the quantity of water contained in it is less. The textures which yield gelatin are, the white fibrous tissue, areolar tissue, skin, serous membranes, and bone; glue, prepared from hides, &c., size from parchment, skin, &c., and isinglass from the swimming bladder of the sturgeon, are various forms of gelatin used in commerce.

Gelatin, obtained by boiling, is in combination with a considerable quantity of water; by a slow and gentle heat this may be driven off, and the gelatin obtained in a dry state. Dry gelatin is hard, transparent, colourless, without smell or taste; of neutral reaction; in cold water, it softens and swells up, and dissolves in warm water. It is insoluble in alcohol and ether, but very soluble in the dilute acids and alkalies. When tannin, or the tincture or infusion of galls, is added to its solution in water, a brownish precipitate is thrown down—the tanno-gelatin, which may be precipitated from a solution of gelatin in 5,000 times its weight of water. Gelatin contains in 100 parts C 50·4 H 7·1 N 18·1 O 23·8 S 0·6.

The process of tanning leather, depends upon the affinity of gelatin for tannin. The skins of the animals, having been first freed from cuticle and hairs by soaking in lime-water, are tanned by submitting them to the action of infusion of oak-bark, the strength of which is gradually increased, until a complete combination has taken place. An insoluble compound is thus formed, capable of resisting putrefaction.

If a solution of gelatin, in concentrated sulphuric acid, be diluted with water and boiled for some time, glycocoll may be obtained from it on saturating with chalk. Again, by boiling gelatin in a concentrated solution of caustic alkali, it is sepa-

rated into *leucine*, $C_6H_{13}NO_2$, and *glycin* or *glycocoll*, $C_2H_5NO_2$. The latter product crystallises in pretty large rhomboidal prisms, is colourless and inodorous.

Chondrin is a substance in many respects similar to gelatin. It is obtained in a state of solution, by boiling water, from the permanent cartilages and from the cornea; also from the temporary cartilages prior to ossification; it gelatinizes on cooling and when dry assumes the appearance of glue. It differs from gelatine, in not being precipitated by tannin, and in yielding precipitates to acetic acid, alum, acetate of lead, and the protosulphate of iron, which do not disturb a solution of gelatin. Chondrin contains in 100 parts C 49·9 H 6·6 N 14·5 O 28·6 S 0·4. Like fibrin and albumen, it contains a minute quantity of sulphur. The interesting researches of Dr. Roudneff, of St. Petersburg (*Archives of Medicine*, vol. iv, p. 304), seem to show that chondrin undergoes conversion into gelatin by oxidation. Prior to the formation of vessels in the temporary cartilage of the embryo, that substance yields chondrin, while, after this, gelatin is obtained from it. Chondrin, obtained from permanent cartilages, was subjected to the action of oxidizing agents, and the resulting mass it is stated gave the reactions of gelatin.

The chemistry of early life differs from that of the embryonic state enormously in the greater activity of the process of oxidation. The functions of Respiration and Circulation are more actively performed, and the quantity of material disintegrated is considerably increased. During the early periods of development there is comparatively slight demand for oxygen. The amount of germinal matter produced is very great, and tissue is being formed and accumulates, but there is no active discharge of function, and the amount of formed material oxidized and destroyed, is very small. Little *work* is performed at this period of life, for *work* results from the disintegration of materials which have been already formed. It is interesting to note how intimately an active condition of the oxidising process is connected with a healthy state and a full working condition of the various organs of the body, and how many morbid conditions of tissues and organs, which necessarily terminate in death, are due essentially to diminished oxidation.

OF THE BLOOD.

As the tissues and organs advance towards maturity, the blood becomes of vast importance, and it is not possible to discuss even cursorily the general chemical changes in the organism without referring to the composition of the blood and the phenomena which are taking place in it during every moment of existence. Although the chemical components of the blood and the blood corpuscles are more particularly considered under *circulation*, it will be necessary to refer briefly to them in this place.

Of the fluids of the body, the blood alone yields the various materials required for the formation of the tissues and organs, and for maintaining them in a state of integrity after their formation is complete; and, through its agency, all the substances resulting from the disintegration of textures which have already performed their work are carried to the different parts of the body at which their removal is effected. The blood must therefore be considered as the medium, by which, at the same time, nutrient matters are carried to every tissue of the body, and products resulting from decay brought to the points at which they can be discharged. The consideration of the chemical changes taking place in the blood will comprise some of the most important chemical phenomena occurring in man and the higher animals during all, except the very earliest periods of existence. The fluid which is concerned in distributing nutrient matter to the tissues of the lower animals, like the blood of man and the higher animals at an early period of development, is perfectly transparent and colourless. It contains some spherical colourless granular masses of germinal matter, which, when at rest, exhibit vital movements. These are the most important and the only constant corpuscles of the blood. The fluid, or *liquor sanguinis*, in which these are suspended, besides water, salts, and fatty matters, contains two very important substances. Of these, one, the *fibrin*, coagulates spontaneously when the fluid is removed from the living organism and brought into contact with any foreign matter. The other, *albumen*, is dissolved in the water, but on the application of heat, or upon the addition of a mineral acid, it passes into an insoluble condition, forming a white clot or coagulum. It is also precipitated

by solution of tannin and by many metallic salts. White or colourless blood corpuscles, fibrin and albumen, which are included in the class of proximate principles (see p. 8), and water, are important constituents of the blood at every period of its existence.

The *white blood corpuscles*, or masses of living germinal matter of the blood, are the direct descendants of the germinal matter of the cells which took part in the first development of vessels. The white blood corpuscle in fact corresponds to the germinal matter in the interior of a 'cell.' There can be little doubt that, at least in those instances in which the nutrient fluid contains no red corpuscles, these colourless corpuscles are the agents concerned in the production of the albumen and fibrin, and there is every reason to believe that the red blood corpuscles, specially characteristic of the blood of vertebrate animals, are formed from these bodies.

It has been already stated that all forms of living germinal matter yield a spontaneously coagulable substance closely allied to the fibrin of the blood, though perhaps not identical with it, and a soluble albuminous material which is precipitated by heat and nitric acid. It is probable that the pabulum required for the nutrition of the higher tissues is prepared and formed through the agency of germinal matter of less special endowments, such as that found in connection with the capillary vessels; and that the free germinal matter in the blood, representing that in the interior of the fully formed cell, itself in its turn grows at the expense of materials formed from other kinds of germinal matter, especially that in connection with the intestinal mucous membrane.

Albumen is so called from the white colour it possesses in its solid coagulated state; 'white' of egg is largely composed of it. Besides forming more than 30 per cent. of the solid matter of the blood, albumen, more or less modified, enters into the composition of many of the tissues of the body. It exists in two states; fluid—being dissolved in the serum of the blood, and in some of the secretions; and solid—forming a large proportion of certain of the tissues; for example, $\frac{7}{12}$ of the dry cerebral substance, which are for this reason called albuminous tissues. These are, the brain, spinal cord and nerves. It also enters into the composition of the muscles, and traces

are found in the aqueous and vitreous humours of the eye. It is present in the various kinds of serum and in pus, poured out under various circumstances, and formed in the course of disease. Albumen contains in 100 parts C 53·5 H 7·0 N 15·5 O 22·4 S 1·6. It exhibits no tendency to assume spontaneously the solid form, except by the loss of the water which is combined with it. By evaporating white of eggs, at a temperature not exceeding 120°, its water is driven off, and solid albumen, in the form of a yellowish transparent brittle mass, is obtained, with all its properties unimpaired. If a solution of albumen, in water, be exposed to a heat between 140° and 150°, it coagulates, and then becomes insoluble in water. Albuminous solutions are alkaline, and it is probable that at least a portion of the alkali is chemically combined.

The mineral acids have the property of coagulating albumen. Of these, the nitric is most used in medical practice. A few drops of this acid will enable us to detect a small quantity of albumen dissolved in a clear fluid, by rendering it more or less opaque. Alcohol also has this property; and hence any albuminous textures submitted to its influence, become hardened and condensed. Bichloride of mercury exercises a similar influence, and is a delicate test for albumen. It was Orfila who first employed this proximate principle as an antidote to the poisonous effects of the bichloride, which combines with the albumen, forming with it an innocuous compound. According to Peschier, the white of one egg is sufficient to render four grains of the poison harmless. Another delicate test for albumen is the ferrocyanide of potassium, which will precipitate it from solution, provided a little acetic acid have been previously added, in order to neutralize the soda in combination with it. Albumen is also precipitated from solution by tannin. It coagulates at the negative pole of the galvanic battery, or at both poles, when a strong battery is employed. Many other reagents will coagulate this principle, but enough have been mentioned for all practical purposes. Albumen is soluble in caustic alkalies. By prolonged boiling in hydrochloric acid albumen is resolved into a substance allied to chondrin. The existence of sulphur as a constituent of albumen, is shown by the blackening of silver that has remained long in contact with it, or by boiling a little albumen in a solution of oxide of lead in potash.

In disease it often happens that albumen is carried off from the system in large quantities in the urine. By any of the means above mentioned, its presence in that fluid may be detected. When heat is used it will always be advisable to ascertain previously whether the urine be acid or alkaline; for the presence of alkali prevents the coagulation of albumen by heat. Hence it is a good rule in testing for this substance to employ both heat and nitric acid. If, however, only one or two drops of nitric acid be added the albumen will be precipitated and then quickly re-dissolved by agitation. This acidulated solution, it must be remembered, is not coagulated by heat. The practitioner should, therefore, be careful never to test albuminous urine in a dirty test tube, which may contain a little nitric acid.* Gigon states that there exists even in healthy urine a substance allied to albumen, and according to Dr. George Harley, the albuminous matter resembles that form of albumen which has been dissolved by gastric juice; for, like this, it is not coagulable by heat or nitric acid.

Paralbumen and Metalbumen are modifications of albumen discovered by Scherer in the fluid of ovarian dropsy and in an albuminous fluid removed by paracentesis. The first is very slightly coagulated by boiling. Alcohol precipitates flocculi, which are re-dissolved by water. The latter is coagulated neither by hydrochloric acid nor by ferrocyanide of potassium. Pancreatin from the pancreatic fluid is closely allied to albumen.

In mammalia it is certain that many different cells can produce a substance which possesses all the chemical characters of albumen. From the cells of cuticle and many other structures a solution can be obtained which contains albumen. The cells of the follicles of the lacteal glands give rise to it, and those which occupy the Graaffian follicles also produce it, and in ovarian dropsy, when these follicles are enormously enlarged, there can be no doubt that the albumen is actually formed in the interior of the cyst, for, as above stated, it differs from the albumen of ordinary serum. Moreover, albumen is found in almost all animals, and in certain of the fluids of plants.

The facts above enumerated render it probable that the

* For the methods of testing albuminous urine, see "Urine, Urinary Deposits and Calculi."

albumen of the blood results from changes occurring in the blood corpuscles. In many cases albumen results directly from changes in germinal matter, but it seems probable that in man and the higher animals, part, at any rate, of the albumen of the blood is formed from the red corpuscles which are themselves formed material resulting from changes occurring in the white blood corpuscles. Albumen is one of the substances which forms the pabulum of cells, and there can be no doubt that from it many very different materials may be produced by the agency of the living or germinal matter of the various textures.

Fibrin exists, in a state of solution, in the blood, forming, with the serum of that fluid, the *liquor sanguinis* of Dr. Babington, in the lymph and in the chyle. It is a constituent of the exudation (coagulable lymph) which forms on certain surfaces, as the result of the inflammatory process, and it sometimes occurs in dropsical fluids.

Fibrin is distinguished from the other substances allied to it by its remarkable property of *spontaneous coagulation*. When blood or fluid containing much fibrin is drawn from a vessel and allowed to rest, it speedily separates into a solid portion, the *crassamentum* or clot, and a fluid portion, the *serum*. The clot of blood consists of fibrin, with the *white* and *red* blood corpuscles entangled in it during its coagulation. It sometimes happens that owing to an unusual aggregation of the red particles together, and to their more speedy subsidence, a portion of fibrin on the surface coagulates without enclosing the colouring matter. A yellowish white layer forms the upper stratum of the crassamentum, and this is called the *buffy coat* or *inflammatory crust*. It is an example of nearly colourless fibrin, but like other forms of this substance, contains also the white corpuscles.

We may obtain fibrin in a state of considerable purity, by cutting the crassamentum into slices, and washing them in clean water so as to dissolve out the colouring matter; or by briskly stirring with a bundle of twigs, blood as it flows from a vessel: the fibrin coagulates upon the twigs in small portions, which being washed, afford good specimens of colourless fibrin; by digesting afterwards, in alcohol and ether, the fatty matters are got rid of. Another mode of obtaining this substance in a

state of purity is that suggested by Joh. Müller. This consists in adding to frog's blood a little syrup (one part of sugar to two hundred parts of water) which retards the process of coagulation for a sufficient time to enable us to filter it. The frog's red particles being too large to permeate the pores of the filter, the liquor sanguinis passes through in a colourless state, and its fibrin coagulates free from colouring matter. Sometimes we obtain masses of fibrin, great part of which is colourless, from the cavities of the heart, and from the large arteries after death. It is also accumulated and disposed in a peculiar lamellar form, in the sacs of old aneurisms.

Pure fibrin is white, tasteless and inodorous; it tears into thin laminæ. Under the microscope it is seen to consist of *a*, fibres crossing one another at every possible angle and interlacing in all directions; and *b*, very numerous white blood corpuscles. It is not yet possible to obtain the fibrinous material in a perfectly pure state and free from the corpuscles. It contracts for some time after its first precipitation, and retains remarkable elasticity, even after it has been for years immersed in preservative fluids. If fibrin be dried it becomes yellow, hard, and brittle, and loses three-fourths of its weight, but imbibes water again when moistened; it is insoluble in both hot and cold water, in alcohol, and in ether. By long-continued boiling in water its composition is changed, and it becomes resolved into a soluble and an insoluble substance, the first of which has been termed the *teroxide* and the second the *binoxide* of protein. Strong acetic acid converts it into a jelly-like mass which is sparingly soluble in water. A solution of nitrate of potash in the proportion of 1 part to 5 of water, readily dissolves fibrin. It is also to some extent soluble in solutions of some other alkaline salts. All the alkalies dissolve fibrin. Any of these solvents of fibrin will prevent the coagulation of blood which has been allowed to drop into it as it flows from the blood-vessels. Fibrin is dissolved by cold concentrated hydrochloric acid, and if kept at a cool temperature for twenty-four hours, the solution acquires an indigo blue colour. Albumen similarly treated assumes a violet colour. Caustic potash, common salt, carbonate of potash and many neutral salts, when mixed in certain quantities with the blood, have the property of retarding or preventing the coagulation of its

fibrin. There still exists much difference of opinion concerning the mode of formation, origin, and uses of this substance.

Dr. Richardson supposed that the fibrin was held in solution by the ammonia present in living blood, but although there is no doubt that this substance will prevent the coagulation of blood, there are many facts opposed to Dr. Richardson's view, and some observers have not succeeded in detecting even traces of free ammonia in fluids in which fibrin existed in its uncoagulated state.

It has been inferred by Mr. Lister that the chemical combination of globulin and fibrinogen, and the formation of fibrin was due to some mysterious and unexplained action of extraneous matters and ordinary solids, upon the previously soluble materials. Others consider that the blood possesses a "natural tendency" to coagulate, but that as long as it remains within the body, if the vessels be in a healthy state, coagulation is prevented. Neither of these views are entitled to be considered *explanations* of the process of coagulation.

Professor Andrew Buchanan, of Glasgow, observed long ago that the fluid of hydrocele yielded a coagulum, if blood serum, probably containing a few blood corpuscles, were allowed to fall into it, although it might be kept for any length of time without coagulation, if no blood serum were added. A. Schmidt, of Dorpat, apparently ignorant of Buchanan's observations made twenty years before, has recently shown that for the formation of fibrin, a *fibrino-plastic substance* of the nature of globulin, must combine with another substance, which he terms *fibrinogen.* Either may be present without the occurrence of coagulation, but if the smallest proportion of the fibrino-plastic compound be added to fibrinogen, coagulation occurs. The fibrino plastic substance is globulin, and may be obtained from various sources, as saliva, synovia, the fluids of the eye, connective tissue, probably also from muscle, nerve, &c. This view concerning the formation of fibrin has been accepted by Mr. Lister.

According to some, the formation of fibrin is a purely chemical process, and results from the direct oxidation of the albumen. Von Gorup-Besanez has shown that ozonized air causes the formation of fibrin-like coagula in an albuminous solution, and that these coagula might be re-dissolved in the

fluid. The researches of Mr. A. H. Smee (*Proceed. Royal Society*, 1863, vol. xii. p. 399), have proved that if oxygen be passed through a solution of albumen, for thirty-six hours, at a temperature varying between 95 and 100° Fah., the solution becomes of firmer consistence, and when examined microscopically, numerous lines indicative of fibres are seen. Mr. Smee infers that the substance thus produced is fibrin, and that it has been formed directly from the albumen by oxidation. He states that it cannot be distinguished from true fibrin by the microscope. But although the new material agrees in many of its characters with what we call fibrin, it is doubtful if it is identical with it. One very remarkable character of fibrin is to contract gradually after its formation, but Mr. Smee has not stated if his fibrin exhibits this property. While the fibrin-like material was being produced, carbonic acid was evolved and phosphoric acid was formed. By the oxidation of gluten, from wheat flour, Mr. Smee also obtained a substance which he could not distinguish from ordinary fibrin. He was unable to obtain fibrin by passing oxygen through urine which contained a large quantity of albumen.

The fact that the quantity of fibrin in blood is increased by oxidation, may be explained, as well by supposing that the oxygen acts upon the matter of the white blood corpuscles, as by inferring that albumen is oxidized; while its absence in certain cases of asphyxia, in hunted animals, and in sudden death by lightning, would be accounted for by the too sudden death of the white corpuscles ensuing in these cases, although it could hardly be attributed solely to deficient oxidation.

We may now consider what may be actually observed under the microscope when fibrin passes from the fluid to the solid state. Observations with the aid of the very high powers ($\frac{1}{25}$ and $\frac{1}{50}$) recently brought into use, have taught us many new and highly important facts which could not have been arrived at without their aid. If the phenomena of coagulation be carefully watched as it occurs under a power magnifying upwards of 2,000 diameters, the following points will be observed in favourable cases soon after the blood has been covered with the thin glass or mica. The first change noticed is, that a film-like appearance is developed in the liquor sanguinis, and this is especially observable in the wake of those

red corpuscles, which are being slowly moved across the field by the currents in the fluid produced by the unequal pressure of the thin glass cover. The appearance may be compared to that seen in the fluid circulating in the cell of vallisneria, except that in this latter innumerable and excessively minute spherical, colourless particles can be discerned; while although many very transparent and scarcely visible corpuscles may be seen in the blood, the fluid does not appear to be almost entirely composed of minute spherical particles, moving about one another as in vallisneria. This film-like appearance is gradually succeeded by the formation of delicate threads, which are seen to cross one another at various angles, and apparently correspond to the lines which the blood corpuscles have traversed as they have moved about the field (plate V, fig. 44). The lines seem to acquire greater density and increase in refractive power for some time after they were first visible. I have never been able to demonstrate that the lines are formed by the actual coalescence and running together of minute particles. It seems to me more probable that the coagulable matter exists in the first instance as a highly diffused plasma, probably formed by the white blood corpuscles, and the smaller colourless corpuscles allied to them, which gradually separates from the serum with which it was originally united, and contracts until it acquires sufficient density and refractive power to be seen by us. During the process of coagulation many of the red corpuscles are seen to become stellate, and these refract more highly, are more dense and are of much less diameter than those which retain their smooth surface, and even, circular, outline. In this change, fluid, containing globulin (?), probably escapes.

That fibrin may be formed *directly from the white blood corpuscles* seems to be proved by the fact that if a white blood corpuscle, which has become attached to a little elevation or depression upon the surface of the glass, be caused to move in one direction away from its point of attachment, it will develop a narrow thread, which gradually increases in length and appears to be drawn out from the corpuscle. It becomes firmer, and more highly refracting. This thread exhibits all the characters of fibrin, and is probably composed of this substance (fig. 45). In many cases the white blood corpuscles throw out exceedingly

thin, thread-like processes, which gradually assume the appearance of filaments of fibrin.*

White corpuscles, which, when first rcmoved from the body, appear perfectly smooth and transparent, gradually bccome more or less granular, plate V, fig. 44, abovc *a*; and the granulcs increase in number and sizc for some time, until the movements exhibitcd by the pcrfectly transparent germinal matter ceasc, and the white corpuscle dies, and forms a coagulum. The fibrin in the blood of some rodents appears perfeetly granular immediately after coagulation has occurred, and there is no indieation of distinct fibres, plate V, fig. 48.

All recently formed fibrin is found to eontain an immense number of thc white blood eorpuscles, as may be readily demonstrated in the beautifully transparcnt colourless coagula not unfrequently found in the cavities of the hcart, plate V, fig. 47. The substance, therefore, which we know as fibrin, undoubtedly eonsists of the highly refraeting, insolublc, and eminently elastic threads (fibrin); and the insoluble transparent mattcr resulting from changcs in the living and eminently mobilc material of the white blood corpuscle.

It seems probable that the threads are originally formed from a substanee produced by the white blood corpuscle. The above observations are not opposed to thc vicw of Buehanan and A. Schimdt,—for the fibrinogen, the material which is required in very large proportion, may be furnished by the white blood eorpuscles and the minute corpuscles of the same nature; while from the red blood corpuscles thc fibrino-plastic substance, of which a mere trace seems to be neccssary, may escapc. The spontancously coagulable matter may, however, in certain cases, remain diffused for months after it has been formcd, without coagulation taking plaee, and then an alteration in the extcrnal conditions, exposure to air, &c., may eause it to assume the solid form.

With refcrenee to the uses of fibrin there ean be no doubt that it performs an important service in limiting hæmorrhage when vessels are divided, and that it forms, when effused in internal parts, or on the surfaee of wounds, a tcmporary tissue,

* "On the germinal matter of the blood, with remarks upon the formation of fibrin."—Trans. Mic. Soc., December, 1863.

COAGULATION OF FIBRINE.

Fig. 44.

a

b

Red and white corpuscles in blood from the finger × 2800 linear. The large smooth circular bodies are the red corpuscles. Three very small red corpuscles are less than the $\frac{1}{8000}$ of an inch in diameter. The smallest particles are composed of matter like that of which the white blood corpuscle (B) consists. Threads of fibrine undergoing coagulation are observed between the corpuscles in the upper and lower part of the field. A, red corpuscle, exhibiting angular projections. Below it, and to the left, is another, with still more pointed processes. September, 1863.

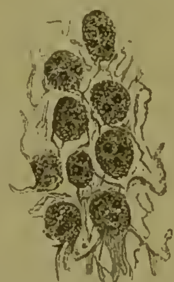
Fig. 45.

White blood corpuscle (human subject), with thread of fibrine connected with it. × 1800

Fig. 46.

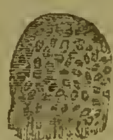
Capillary vessel from the mucous membrane of the epiglottis from a man aged 74. × 700.

Fig. 47.



From a pale clot in the heart of a patient who died of exhaustion, showing white corpuscles and fibres of fibrine × 700

Fig. 48.



Portion of a large mass of fibrine from Guinea pig's blood the instant coagulation had occurred. × 1800

$\frac{1}{1000}$ of an Inch × 700.

" " × 1800.

$\frac{1}{10000}$

" " × 2,800.

$\frac{1}{10000}$

a cementing or protecting substance, or bond of union, between separated parts, which serves as a nidus for the development of the masses of germinal matter which are to take part in the formation of a higher, more elaborate, and more slowly formed, but much more durable texture. It has been suggested that fibrin is required for the nutrition of a special class of textures, as the gelatin-yielding tissues, but we find fibrin in cases in which there are no such textures; and where these tissues do exist, they require such a small amount of nutrient matter, and undergo such slight change, that we should scarcely expect to find the proportion of fibrin, which exists when the formation of these tissues is complete, as great as it is. Nor is it probable that such highly important elements of the blood, as the white blood corpuscles, should take part in the nutrition of any one special tissue; and if upon other grounds than those advanced we were disposed to accept such a view, we should hardly be inclined to assign to such highly important and peculiar bodies the office of nourishing the lowest and simplest tissue in the body. Upon the whole, the facts known render it more likely, as has been before advanced, that the various masses of germinal matter of the several textures, form, from the same nutrient materials compounds different in structure, property, and composition; than that substances allied to the tissue to be formed, are simply selected, separated, and deposited from the nutrient plasma. There is indeed no evidence of the existence of many different substances in the blood of man and the higher animals, in which the number of different textures and secretions is very great.

Red Blood Corpuscles.—The blood of vertebrate animals contains numerous coloured corpuscles, which are known as the red blood corpuscles, and these contribute to the blood its most important characteristics. The red colour of blood is entirely due to these bodies, and the difference in colour between arterial and venous blood is caused by alterations occurring in the material of which the red corpuscle is composed.

These corpuscles are probably derived from the white ones, so that the younger red blood corpuscles contain germinal matter, a fact proved by the circumstance, that in some instances, under high magnifying powers, this germinal matter has been seen to

move away from the coloured material already produced.* A the corpuscle advances in age, the whole of the germinal matter becomes converted into the coloured lifeless formed material which very readily assumes the crystalline form. The red corpuscle, in fact, seems to be composed of a small portion of soft matter, of a viscous consistence, very slightly soluble in fluid, but capable of undergoing solution in the serum under certain circumstances. In some animals the red matter retains its colloid semi-fluid state only while it is kept in active motion in the circulation. The red blood corpuscles of the Guinea-pig pass into a crystalline state within half-an-hour after they have been removed from the vessels, and without the addition of any reagent or solution whatever. It is certain, at least in this case, that there is no rupture of membrane and escape of contents. The small mass of viscid matter of which each single corpuscle is composed may be seen to form a single crystal, while if the corpuscles be slightly warmed, they break up into many small portions, each one of which assumes the tetrahedral form.* (See plate VI, fig. 49; plate VII, figs, 58 to 61.)

It appears probable that the coloured material of which the fully-formed red blood corpuscle is composed is a lifeless chemical substance, which, under the conditions to which it is exposed during the circulation, becomes resolved into certain compounds which are of great importance in nutrition, and others, which being readily soluble in fluid, with a high power of diffusion, or in a gaseous state, are readily removed from the organism altogether.

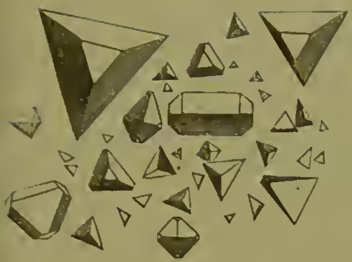
It was formerly considered that the matter which enters into the formation of the red blood-corpuscle consisted of two substances, hæmatin and globulin, but later researches rather tend to the conclusion, that in the natural condition there is one chemical substance which, however, is readily decomposed. This has been termed *Globulin*, *Hæmato-globulin*, *Hæmato-crystallin*, and *Hæmo-globulin*. It is the crystallisable material above referred to. Various forms of hæmato-crystallin, from the Guinea-pig, human subject, cat, and mouse, are represented in plate VII.

A solution of this substance, as well as of certain products of its decomposition, produces peculiar absorption-bands in the

* Observations on the Red Blood Corpuscle. Trans. Mic. Society, Dec. 1863.

BLOOD CRYSTALS.

Fig. 49.



Blood crystals. Guinea Pig. × 215.

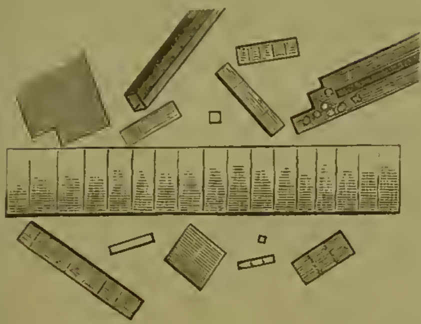
Fig. 50.

Human blood crystals. × 215

Fig. 51.

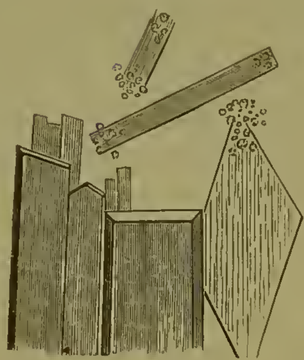
Crystals of hæmatoidin from human liver. × 215.

Fig. 52.



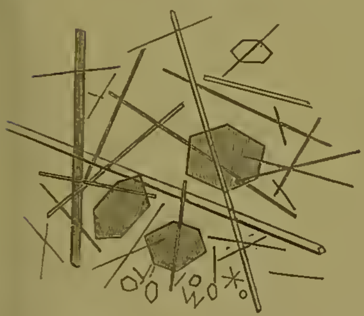
Blood crystals Human. × 215.

Fig. 53.



Blood crystals. Cat. × 215.

Fig. 54.



…d crystals. Mouse

Fig. 55.

HÆMIN CRYSTALS.

Human. × 215.

Pig. × 215.

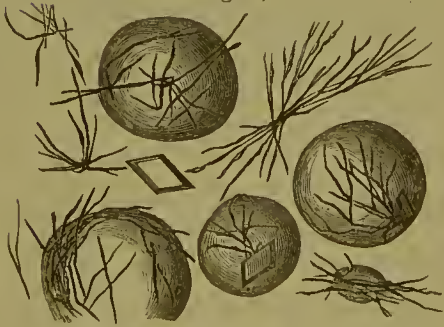
Toad. × 215.

Goldfinch. × 215.

Fig. 56.

Feathery crystals of hæmatin, found in the urine a fortnight after slight rupture (?) of one kidney. Human subject. × 215.

Fig. 57.



Rhomboidal and feathery crystals of hæmatin, from a softened clot. Human × 215.

B.]

$\frac{1}{1000}$ of an Inch × 215.

[To face p. 126.

solar spectrum. Hoppe was the first to demonstrate this interesting fact, and found that a very dilute solution of blood was sufficient for the purpose. The same bands were produced by the blood of different animals. Stokes proved that this colouring matter was capable of existing in two states of oxidation, and that a very different spectrum was produced according as the substance which he termed *cruorine* was in its more or less oxidised condition.* Protosulphate of iron,† or protochloride of tin, causes the reduction of the colouring matter, and by exposure to air oxygen is reabsorbed, and the solution again exhibits the spectrum characteristic of the more oxidised state. In venous blood there is reason to believe that part of the cruorine exists in its purple or less oxidised condition, and that this, in passing through the lungs, is reoxidised and converted into the scarlet cruorine, plate VII, figs. 62 to 65.

The different substances obtained from the normal blood colouring matter produce different bands. Thus, *Hæmatin* gives rise to a band in the red of the spectrum between the lines C and D. *Hæmato-globulin* produces two bands, the second twice the breadth of the first in the yellow portion of the spectrum between the lines D and E. The absorption bands differ according to the strength of the solution employed, and the medium in which the blood salt is dissolved;‡ but an exceedingly minute proportion dissolved in water is sufficient to bring out very distinct bands, and in his new spectroscope Mr. Sorby is able to obtain the band from a single blood corpuscle.§

The most important chemical compounds obtained from the red blood corpuscles are the following:—*Hæmatin*, *Hæmatoidin*, and *Hæmin*.

Hæmatin may be obtained from *hæmato-globulin*. It occurs in old extravasations of blood, and may be detected in the fæces.

* "On the reduction and oxidation of the colouring matter of the blood," by G. G. Stokes.—Proceed. R. S., 1864, vol. xiii, p. 355.

† The solution is made as follows. To a solution of protosulphate of iron, enough tartaric acid is added to prevent precipitation by alkalies. A small quantity of this solution made slightly alkaline by ammonia, or carbonate of soda, is to be added to the weak solution of blood in water.

‡ On this subject the most recent observations will be found in F. Hoppe-Seyler's Handbook of Physiological and Pathological Chemistry. Hirchwald. Berlin, 1865. This work is a very valuable one.

§ "On the construction and use of the Spectrum Microscope," by H. C. Sorby, F.R.S.—Pop. Science Review, January, 1866.

It is not crystalline, and when dry it forms a brown powder, which contains nearly 9 per cent. of iron. A thin layer of a solution of hæmatin exhibits a greenish colour, while a thick one is dark red. Hoppe-Seyler names another substance allied to *Hæmatin*, *Methämo-globulin.* This may be a mixture of hæmatin and some albuminous substance.

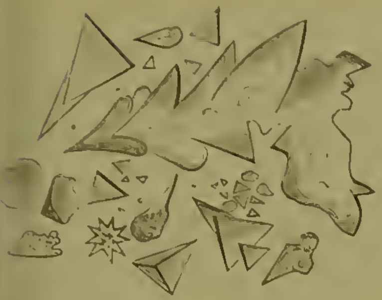
Hæmatoidin is a modified form of hæmatin. It is not easily decomposed, is insoluble in water, alcohol, ether, and acetic acid, but readily soluble in alkalies. This is the substance which is found in old clots and extravasations, and not unfrequently in the walls of some of the smaller vessels, perhaps marking the situation of old hæmorrhages. It crystallises in very beautifully defined rhombic crystals, plate VI, fig. 51. It also forms long filaments, and not unfrequently slightly curved elongated crystals collected into bundles, which sometimes take the form of oval or dumb-bell shaped masses, plate VI, figs. 56, 57. This substance seems closely allied to a yellow crystalline material obtained from the bile. It would indeed be very difficult to distinguish hæmatoidin crystals found in clots from some crystals which have been produced in biliary matters. Hæmatoidin may therefore be the same substance as that obtained from bile under the names Cholepyrrhin Biliphæin, Bilifulvin, and more recently Bilirubin. Zenker and Funke have shown that from the yellow crystals of bilifulvin red crystals of hæmatoidin may be obtained.

Hæmin is a substance which was discovered by Teichmann. It is obtained artificially from hæmatin and hæmato-crystallin. By the addition of a little glacial acetic acid to a small portion of clot of blood, the hæmin is produced and crystallises in rhombic scales. Hæmin crystals may be thus obtained from the red blood of man and the lower animals. Blood that has been kept for some time yields these crystals as well as fresh blood, and, with care, they may be obtained from the smallest blood spot on clothes, &c., hence this reaction is of value in medico-legal inquiries, but, as a test, it is less delicate than the spectrum analysis already referred to. Hæmin crystals from the human subject, pig, toad, and goldfinch are represented in fig 55.

Extractive Matters.—It is probable that the so-called extractive matter of blood consists of substances which result during

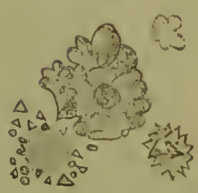
BLOOD CRYSTALS. CRUORINE. CAPILLARIES.

Fig. 58.



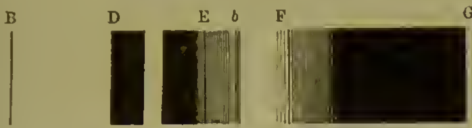
...ood crystals from the blood of the Guinea pig. × 700.

Fig. 59. Fig. 60.



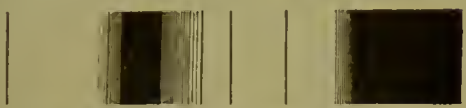
Disintegration of red blood corpuscles of Guinea pig's blood, and formation of crystals. After application of a gentle heat × 700.

Fig. 62.



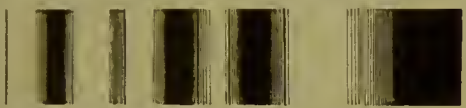
Absorption bands. Arterial and scarlet cruorine.

Fig. 63.



Absorption bands. Venous blood and purple cruorine.

Fig. 64.

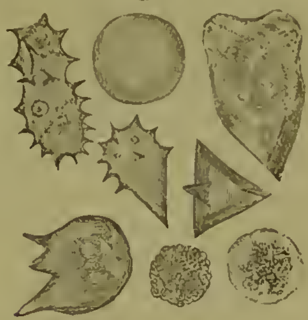


Absorption bands. Blood treated with acetic acid.

Fig. 65.

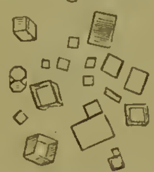
Absorption bands. Solution of hæmatin. Copied from Stokes. Proc. R. S., 1864.

Fig. 61.



Formation of blood crystals from the red blood corpuscles of Guinea pig's blood, shortly after removal from the body. No reagent added or heat applied. × 1800.

Fig. 66.

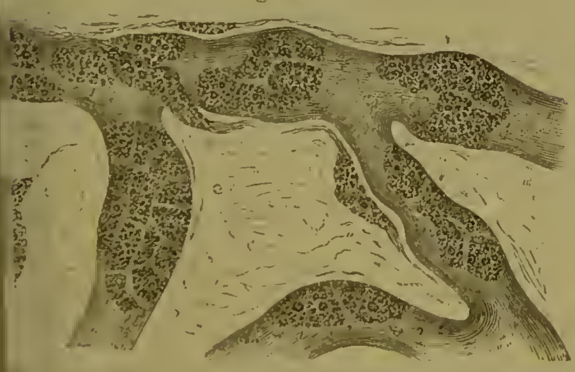


Chloride of sodium

Fig. 67.

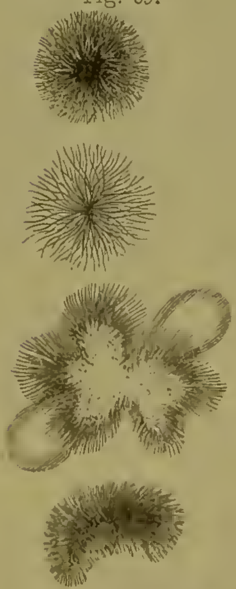
...pillary showing masses of germinal matter projecting into its interior. Areolar tissue Mouse. × 700

Fig. 68.



...ary connective tissue Cattle plague. The masses of germinal ...r of the capillary are very much enlarged, and are dividing and subdividing to form new masses. × 700.

Fig. 69.



Margarine crystallised spontane... After Robin and Verdeil.

$\frac{1}{1000}$ of an Inch × 700.

" " × 1800.

$\frac{1}{10000}$

[To face p ...

the decay and disintegration of the blood corpuscles, and their resolution into various definite compounds. These indefinite extractive matters probably pass off in an altered form in the urine and other secretions almost as fast as they are produced, for the quantity of extractive matter in normal blood is very small, scarcely amounting to more than ·5 or ·6 per cent., but in certain morbid conditions a much larger proportion is found.

Of the *saline* constituents of the blood taking part directly in the nutrition of tissues, or subservient thereto, probably the chlorides and alkaline and earthy phosphates are the most important. The chlorides increase the fluidity of an albuminous fluid, and probably facilitate the access of the nutrient pabulum to the germinal matter of the cell. In all cases in which cell-development is going on actively a large quantity of common salt is present. During the development of the normal tissues in the embryo, and during the multiplication of the masses of germinal matter in disease, as in pneumonia, the formation of abscess, in cancer, and other morbid states, characterised by rapid cell growth, chloride of sodium is to be detected in considerable proportion. It is doubtful if the alkaline phosphates are devoted to nutrition, although there can be no doubt they are of service in giving to the serum an alkaline reaction, and are, perhaps, to some extent, concerned in the absorption of carbonic acid and other changes. The greater part of the phosphate in the blood is probably derived from the bread and meat taken in the food. The earthy phosphate of lime which forms 3·5 per cent. of the ash of blood is an important substance. *Iron* should also be enumerated among the saline constituents of the blood, of service in the nutritive process, but we are not yet acquainted with the exact part it plays in the chemistry of the body. The foregoing are probably the constituents of the blood which take part in the nutrition of the various textures, and from them the chemical compounds found in the tissues and entering into the composition of the various secretions, are alone formed.

There are many other substances in the blood, which probably result from the action of oxygen upon certain of the constituents of that fluid or of the tissues, and are poured into the blood prior to their further oxidation and ultimate removal from the organism by the agency of various excretory organs.

From an albuminous fluid of comparatively simple composition, but undergoing constant change by the action of oxygen upon certain of its constituents, textures and organs of very elaborate structure, capable of performing complex functions, are constructed, but, indirectly, through the agency of germinal matter.

The highly important part which the blood plays both in the nutrition and disintegration of the textures of man and the higher animals cannot be advantageously discussed, unless the general nature of the changes effected in it and in the textures, by the process of oxidation, is referred to in the first place. We may then allude to the operations occurring simultaneously in different parts of the organism under the two following heads:—the production of peculiar compounds in the tissues and organs, from certain constituents of the blood of a very different composition:—the manner in which new substances are added to the blood to take the place of those which have been removed from it and appropriated.

OF THE CHANGES EFFECTED BY OXIDATION.

By the direct or indirect action of oxygen upon certain constituents, soluble matters fit for appropriation by the germinal matter of the several tissues are prepared, while at the same time insoluble substances which are to be got rid of are converted into highly soluble compounds, which are easily removed from the body. It has been very generally concluded that oxygen is directly concerned in the processes of nutrition and growth. But many considerations render it probable that it is required in greater proportion for the conversion of products resulting from death and decay into chemical compounds which may be readily and quickly removed from the organism, by which the access of new pabulum to the germinal matter is facilitated, than for the direct nutrition and increase of the germinal matter itself. Oxygen is to be regarded as a destroyer of compounds already formed, not as a pabulum. It seems subservient to the process of disintegration rather than to that of construction. It has been observed that the activity of cell growth and multiplication is remarkable at an early period of development when the process of oxidation is far less active than in the fully developed state. The organs in which these processes are most active in the adult are

remarkable rather for a very limited, than for a very free, supply of oxygenated blood. In the case of morbid growths, like cancer, which are remarkable for rapidity of growth, the supply of arterial blood is often very small. In acute inflammation of the lung, the air cells become rapidly filled with "lymph," the formation of which is dependant upon minute masses of germinal matter, and these have grown and multiplied under conditions which were quite incompatible with free oxidation. Lastly, we shall find that the anatomical distribution of the small arteries to certain secreting organs and their arrangement in the muscular and nervous tissues is such as to render it more probable that the arterial blood which they carry, takes part in the process of oxidation and disintegration of materials already formed, than that it is connected with nutritive operations.

Although there can be no question concerning the great importance of oxygen in the changes taking place in living beings, we are still in doubt as to the precise manner in which this oxygen acts, and the particular substances with which it combines. It is possible that the oxygen may be in some peculiar state of combination before it acts, for it is well known that many substances which are not affected by free oxygen, readily combine with this substance, if it be already in a state of combination.

The absence of red blood corpuscles from the blood of many invertebrate animals proves conclusively that these bodies are not essential to the process of oxidation. All the nutrient juices which permeate the various tissues hold oxygen and carbonic acid gases in solution, and it is certain that in some cases the action of oxygen is brought about solely by its aqueous solution. While on the other hand, it has been conclusively shown that oxygen is directly absorbed and carbonic acid evolved by the tissues as well as by the blood; and the experiments of G. Liebig have proved that frogs' muscles continue to absorb oxygen and give off carbonic acid even after their removal from the body. It is therefore certain that neither for the absorption of oxygen nor for the production of carbonic acid, are the red blood corpuscles essential, but that chemical combination takes place between the oxygen and certain elements of the tissues. It is not possible, however, to

state confidently whether combination actually occurs in the tissue itself or is effected only through the agency of the masses of germinal matter so abundant in every tissue, and found in connection with the capillary wall. With regard to muscle it must not be forgotten that upon the surface of each elementary muscular fibre are numerous delicate nerve-fibres, having many masses of germinal matter connected with them, and it is therefore at least possible that the process of oxidation may be taking place in connection with this tissue instead of in the interior of the contractile material, as is generally supposed. If the oxygen combines with or decomposes substances entering into the formation of the tissues, or immediately resulting from their disintegration, the process is merely a chemical one, and might, one would think, be imitated out of the body, but if only with matters resulting from the immediate disintegration of germinal matter, it cannot be so easily explained, and the change may perhaps be due to the elements coming into contact with the oxygen in some very peculiar state.

If the fluids distributed to the tissues in which active changes are taking place are only imperfectly charged with oxygen, or if, although fully saturated, there be some impediment to their free circulation through the tissue, imperfectly instead of fully oxidised substances result, which, from being insoluble or only slightly soluble, cannot be readily removed from the seat of their formation, and if these conditions interfering with free oxidation, persist, such insoluble compounds accumulate. Not only do such substances impair the action of the tissue in which they are deposited, but they interfere, to some extent, with the equable distribution of fresh nutrient material. In the process known as *fatty degeneration* the substances resulting from the disintegration of the tissue under the influence of a too limited supply of oxygen, accumulate in its texture and seriously impair its action. In many cases not only is the existing tissue rendered soft and rotten, and prone to give way, but the process of formation of new tissue to take its place is partly or entirely suspended.

The activity of the process of oxidation seems to be increased by the presence of alkali, as is well known to be the case with the oxidation of organic matters out of the body. In cases in which the quantity of alkali in the blood is less than normal,

various substances in that fluid are not fully oxidised, and the so-called extractive matters, together with uric and oxalic acids, and allied compounds, result, instead of the more soluble highly oxidised substances, such as urea and carbonic acid, which are so readily removed from the system in the excretions. The value of alkalies and of their salts with the vegetable acids, in all those conditions which are characterized by the formation and accumulation in the blood, or tissues, of imperfectly oxidised substances, is well known to all practical physicians. The blood and the fluids which bathe the tissues in health exhibit an alkaline reaction, due to the presence of soda in combination with albumen, and with carbonic and phosphoric acids. It is probable that substances resulting from the biliary matters exert an influence similar to that of alkalies, and perhaps perform a very important office in facilitating that intimate contact between elements having a strong chemical attraction for one another, which immediately precedes chemical action.

It has been sometimes imagined that oxygen at once combines with the carbon of certain constituents dissolved in the blood or fluids, or even entering into the composition of the solids of the tissues, but it is very unlikely that this should be the case. Although the present state of chemical knowledge has led chemists to infer that in the body highly oxidised products result from the combination of successive portions of oxygen with the same substance, so that portions of hydrogen and carbon are successively removed, until a highly complex organic compound is reduced to one of a comparatively simple composition, and finally into the raw materials of organic life, carbonic acid and water, it is extremely doubtful if chemical changes occur in this manner in the organism. A process of the kind has indeed been performed in the laboratory;* for

* An example of this degrading oxidation is afforded by the action of oxidising ents upon glycol (a chemical analogue of alcohol).

Glycol	$C_2H_6O_2$
Glycolic acid	$C_2H_4O_3$
Glyoxal	$C_2H_2O_2$
Glyoxalic acid	$C_2H_2O_3$
Oxalic acid	$C_2H_2O_4$
Formic acid	$C\ H_2O_2$
Carbonic acid	$C\ \ O_2$
Water	H_2O

These substances, with the exception of glycol, are also formed by the decompo- on of nitrous ether ($C_2H_5NO_2$) in contact with water.—[Note from Prof. Bloxam.]

example, by subjecting certain complex chemical substances to oxidising agents, bodies are obtained "in which the number of the constituent atoms of hydrogen and carbon becomes progressively less and less, until we arrive at bodies containing only two, and finally at bodies containing only one carbon atom."

By oxidising stearic acid $C_{18}H_{36}O_2$ with nitric acid of moderate strength, the following bodies are obtained :*

	Oxidation Products.	
Rutic acid	$C_{10}H_{20}O_2$	
Suberic		$C_8H_{14}O_4$
Œnanthic	$C_7H_{14}O_2$	
Pimelic		$C_7H_{12}O_4$
Caproic	$C_6H_{12}O_2$	
Adipic		$C_6H_{10}O_4$
Butyric	$C_4H_8O_2$	
Succinic		$C_4H_6O_4$

It must however be borne in mind that no evidence has yet been adduced of the occurrence of this successive modifying action of oxygen in the animal body. The chemist observes in the laboratory that a substance under the influence of oxidising agents gradually descends in the scale of complexity as the oxygen successively burns off portions of its hydrogen and carbon; but it seems much more probable that the formation of the chemical substance in the animal body is due to the action of oxygen upon germinal matter, and that, so far from there being a series of changes, a highly, moderately, or slightly oxidised substance results, according to the conditions present when the change occurs. The facts of the case render the chemical view of successive oxidations untenable. There is no good reason for believing that starch as starch, sugar as sugar, or fat as fat, unites with oxygen in the body. The theory that several chemical compounds must be produced between the starch, sugar, or fat on the one hand, and the carbonic acid on the other, is merely a chemical hypothesis, for which as yet no very good grounds exist, since no one has produced these intermediate bodies by causing oxygen to unite directly with any of the above substances, and such intermediate products have not been satisfac-

* Odling's Lectures on Animal Chemistry. 1866. P. 48.

torily traced in the animal body; while anatomical facts render it more probable that in the disintegration and removal of *all* textures germinal matter is intimately concerned, and that instead of oxygen acting directly upon the materials of the texture these are first taken up by germinal matter which in its turn is destroyed, giving rise to the substances which are usually considered to result directly from the disintegration of *tissue.*

Of the carrying of Oxygen to all parts of the Body.—The red blood corpuscles of vertebrate animals are the agents principally concerned in carrying the oxygen introduced into the organism by respiration, to different parts of the body. They also take up carbonic acid from the tissues and deliver it at the pulmonary surface where they receive the oxygen in exchange. The material of which the red blood corpuscles are composed possesses in a remarkable degree, as has been already stated (page 126), the property of absorbing and parting with oxygen and carbonic acid gases. Fernet (Comptes rendus, August 2nd, 1858) showed that blood corpuscles absorbed twenty-five times as much oxygen as the same quantity of water, and that the oxygen could be again expelled in vacuo at 98° F. This temporary fixation of gases by the material of the red blood corpuscles is interesting, and, as is well known, other substances behave in a similar manner towards gaseous bodies; for instance, ferrous sulphate will take up nitric oxide, which it again gives up in vacuo. Cuprous chloride takes up carbonic oxide, which may be disengaged from it by boiling. One per cent. of common phosphate of soda enables water to absorb twice the normal proportion of carbonic acid, which may be expelled by agitation with air. And many other examples of bodies possessing similar properties might be adduced.

It is probable that some of the constituents of the red blood corpuscles undergo oxidation, and, perhaps, in this way a certain proportion of urea, carbonic acid, and other substances may be *formed;* while in cases where the oxidation is imperfect, uric, oxalic, lactic, and perhaps other incompletely oxidised bodies may result. The property exerted by the blood corpuscles of absorbing gases is, however, greatly influenced by various agents, and there can be little doubt that the deleterious effects of many poisons are due to the influence they exert upon the absorption and removal of carbonic acid. The experiments

of Dr. George Harley have shown that *snake poison*, *uric acid*, and some other substances accelerate the absorption of oxygen and the exhalation of carbonic acid; while *sugar*, *hydrocyanic acid*, *nicotine*, *morphine*, *chloroform*, and *alcohol* exhibit a contrary effect, and diminish the property which the constituents of the red blood corpuscles exhibit to unite with oxygen and give off carbonic acid.* The action of oxygen on *cruorine* has been referred to in page 127.

Besides the property of acting as carriers of ordinary oxygen, it is possible that the red blood corpuscles may be very efficient carriers of *ozone*. This opinion has been adopted by His and other observers, who state that they readily take up and give off this peculiar form of oxygen which possibly is instrumental in combining with certain products resulting from the decay of animal substances, and thus preventing their deleterious action in the organism; but, at the same time, it should be remarked that at present we know very little of a positive nature concerning ozone or its actions.†

Relation of Oxidation to the heat producing process.—Not only has the development of heat in the animal body been attributed to the combination of oxygen with carbon and hydrogen of some of the constituents of the blood and tissues, but it has been concluded that in all cases in which the temperature of the body rises above the normal standard the activity of the oxidising process must be necessarily augmented; and this notwithstanding the fact well and widely known, that certain states of disease, remarkable for an elevated temperature, are associated with conditions seriously interfering with the free introduction and distribution of oxygen. The fact that the temperature of the body has been known to rise several degrees after death, in diseases in which for some time previously the introduction of oxygen into the blood had been seriously

* Proceedings of the Royal Society, 1864.

† Much difference of opinion still exists concerning the nature of ozone. Schönbein considers that oxygen exists in three different allotropic conditions, of which, two are active and opposed to each other; these are *ozone* and *antozone*, equal quantities of which neutralize each other and form inactive or *neutral oxygen*, which may be separated one-half into ozone and one-half into antozone. Neither ozone nor antozone, have however, yet been isolated in a state of purity, but are always mixed with neutral oxygen. It appears that Brodie discovered the polar condition of oxygen, and his views were applied to ozone by Schönbein about ten years afterwards.—(See Proc. Roy. Soc., vol. xi. p. 442.)

interfered with, would seem to be fatal to this view, although it is still widely accepted and taught.

In all those conditions of system which are accompanied by an elevation of the temperature there is an increased production of germinal matter of the tissues of the body generally, while in cases in which there is a local increase of germinal matter, as in the formation of a common abscess, there is invariably a rapid evolution of heat. In both conditions the activity of the oxidising process is far below the healthy standard, while the temperature is many degrees above the normal range, and it is therefore impossible to resist the inference that the elevation of temperature is due rather to changes accompanying the increase of this germinal matter than to increased oxidation. The elevation of temperature is, in fact, associated with suboxidation, and therefore cannot, as has been affirmed, be dependent upon per-oxidation. We must not omit to notice that it has been recently shown by Berthelot that, by the hydration and dehydration of organic substances heat results.* Thus, sugar, starch, and fatty matter, by decomposition give rise to increased development of heat; and when albuminoid matters are hydrated and decomposed, or dehydrated and caused to enter into combination, heat is set free altogether independently of the process of oxidation. And, lastly, it has been demonstrated by MM. Estor and St. Pierre (Mémoires de la Société de Biologie, 1865) that the venous blood returning from an inflamed part is of a brighter tint than ordinary venous blood, and contains sometimes more than twice as much oxygen. So that, although the temperature is several degrees higher than in the normal state, these observations prove that less oxygen is consumed.

Many facts would indeed justify the inference that the red blood corpuscles are more intimately concerned in the carrying away and distribution of heat, and thus in equalising the temperature in various parts of the body, than in the actual production of heat. Supposing heat to be set free during the increase of the germinal matter of the capillary walls, which is associated with its increase in adjacent tissues, as in an ordinary case of inflammation, the effect of the corpuscles coming into contact one after the other with the enlarged masses of germinal matter, as they traverse the capillaries, would be to carry

* Mémoires de la Société de Biologie, 1865.

away the increased amount of heat and diffuse it over the system. In this way a plausible explanation is afforded of the great importance of keeping up the heart's action in diseases characterised by a considerable elevation of temperature, the beneficial effects of which have been demonstrated by observation and abundantly confirmed by experience.

Of the substances resulting from the action of Oxygen upon constituents of the Organism.—It is proposed to refer in this place very briefly to a few only of the many compounds which are formed in the organism by oxidation. Many others will be alluded to when the various liquid secretions in which they are found come under consideration.

The *action* of organs is in great part dependent upon oxidation, and the amount of texture destroyed; and the quantity of oxygen required for the formation of oxidised products varies according to the intensity of the action. In many cases the degree of activity, or the actual amount of *work* performed within a given time, can, in fact, be measured by estimating the amount of oxidised substances produced. By the artificial oxidation of certain albuminous matters, oxidised products similar to those found in the body may be formed. Van Deen states that, by the action of nascent oxygen developed from water by a constant current of electricity, he succeeded in obtaining urea, uric acid and allantoin from *albumen*, and the two first from *gelatin*; sugar and lactic acid from glycerine and from inosite; and urea and allantoin from uric acid. Many of these bodies, he says, may also be obtained by the action of ozone upon the same substance, and it is probable that the electrolytic ozone is the real agent in the above experiment.

It has been stated that a great number of the substances found in living beings have been produced in the laboratory, and that there is reason to think that eventually every one may be artificially built up. When, however, the various instances which have been adduced are carefully investigated, it is surprising how the number usually advanced becomes reduced, and it is indeed difficult to point out a single product proved to result immediately from direct tissue oxidation, which can be formed synthetically from substances taken exclusively from the inorganic kingdom,* and the least consideration will satisfy

* Berthelot's synthesis of formic acid from carbonic oxide derived from carbonate

any one that so far from the conditions under which compounds are formed in living things resembling those present when similar substances are produced in the laboratory, they are totally different. There is not indeed, as far as is yet known, the slightest real analogy between the chemical operations in the laboratory and those taking place in living germinal matter.*

Urea (CH_4N_2O). Among the substances probably resulting from the oxidation of compounds allied to albumen, one of the most important is urea. This is a crystalline excrementitious substance, very soluble in water, and readily diffusible. In health it is separated from the blood as it passes through the vessels of the kidney so fast that only mere traces can be detected, even if a large quantity of healthy blood be operated upon. But if the action of the kidneys is impaired by disease, or if the organs are extirpated, or if a ligature be passed round the artery, so as to prevent the blood from passing through the kidney, urea may accumulate in the blood in sufficient quantity to be detected in the serum without difficulty. Urea is not found in the muscles, although it can be obtained by the decomposition of kreatine and other substances found in muscular tissue. Recent researches have rendered it probable that much of the urea which is excreted is not *formed* in the tissues or in the blood, and merely separated and eliminated by the kidney, as was formerly supposed, but that a considerable proportion is actually produced in the kidney itself. It seems probable that the oxygen dissolved in the water which filters away from the arterial blood as it slowly traverses the capillaries of the Malpighian tuft, oxidizes certain constituents of the cells which line the uriniferous tubes, and that urea is one of the substances resulting from this action. It would appear that for the formation of urea in quantity a large proportion of fluid is necessary, and in the case of animals living under conditions which interfere with the introduction into and passage through the system of large quantities of water, uric acid, and other less soluble substances seem to be substituted for urea. Crystals of urea are represented in plate VIII, fig. 70.

of baryta by the action of iron at a high temperature, does seem to be entirely independent of organic life.

* See papers in the Medical Times and Gazette, especially April 7th and 14th, 1866.

Uric Acid ($C_5H_4N_4O_3$), plate VIII, fig. 71, is a substance less highly oxidised than urea, and there are reasons for believing that the latter is formed from it by oxidation. The proportion of uric acid increases under various conditions, in which the oxidising operations are interfered with, or imperfectly performed. It has been detected by Dr. Garrod in the blood and other fluids of gouty patients, in decided quantity, and it may be regarded as one of the products of incomplete oxidation. In birds and certain reptiles the renal secretion consists principally of salts of uric acid. By the formation of urate of ammonia a considerable proportion of the waste carbon is removed by the kidneys of birds, instead of nearly the whole being exhaled by the pulmonary surface. Dr. Odling remarks that the lungs of birds are required to discharge only $\frac{3}{4}$ instead of $\frac{7}{8}$ of the carbon resulting from the metamorphosis of nitrogenous tissue, as in animals. "On this view, the comparatively large kidneys of birds and insects will have reference not only to the absolute amount of tissue metamorphosed, but also to the relative increase in the proportion of carbon excreted by their kidneys to that excreted by their lungs."

Hippuric Acid ($C_9H_9NO_3$) is found in large quantity in the urine of the horse and many graminivorous animals, and seems to be formed under the conditions which, in carnivora, lead to the production of uric acid. Hippuric acid is formed in the human organism, and is always present in the urine. According to Weismann and Hallwachs, nearly thirty-five grains are excreted by a healthy man in twenty-four hours. The researches of Kühne and Hallwachs render it probable that hippuric acid is produced from the glycocine formed in the liver. Crystals of hippuric acid are figured in plate VIII, fig. 72.

Leucine ($C_6H_{13}NO_2$) and *Tyrosine* ($C_9H_{11}NO_3$). Among the substances resulting from the oxidation and decomposition of albuminous matters in the body, and capable of being formed in the laboratory artificially, are two bodies, leucine and tyrosine, which are of great interest. They may be obtained from all substances allied to albumen or gelatine by prolonged boiling with mineral acids or alkalies. Dr. Odling has well remarked that these two apparently opposite processes are the same in principle. "In each case the acid, or alkali, merely enables the protein or gelatinoid substance to react with water

whereby one portion of it becomes oxidised into leucine, tyrosine, &c., while another portion is hydrogenised into divers products." Leucine and tyrosine cannot be built up synthetically from inorganic matter. They have been found in the normal tissues and secretions in small quantity ; but in diseases in which certain physiological processes are seriously deranged they are found in comparatively large proportion. This is particularly the case in certain diseases of the liver, as was shown by Frerichs. Not only may both substances be detected in the liver after death from acute yellow atrophy of that organ, and some other affections, but large quantities are often excreted in the urine during the patient's life.

Leucine has been detected in the saliva, pancreatic fluid, bile and urine. It is present in the intestinal glands and in the spleen pulp, and it has been obtained from the thymus, thyroid and lymphatic glands. Bœdeker states that leucine is an ordinary constituent of pus. In most cases, tyrosine is associated with the leucine. Both substances have been obtained from the tissues of many of the lower animals; and from the cochineal insect tyrosine may be obtained in quantity, as was first proved by De la Rue. And there can be no doubt that they are much more widely distributed than was formerly supposed. They have not yet been detected in muscular or nervous tissue. Leucine crystals are seen in plate VIII, fig. 76.

The various substances resulting from the oxidation of starchy and saccharine substances and fatty matters will be considered in the proper place. Among these, perhaps water (H_2O), oxalic acid ($C_2H_2O_4$), acetic acid ($C_2H_4O_2$), mucic acid ($C_6H_{10}O_8$), butyric acid ($C_4H_8O_2$), and succinic acid ($C_4H_6O_4$), are the most important. It is probable that when the process of oxidation is fully performed, carbonic acid is produced in place of these less highly oxidised organic acids.

OF THE FORMATION OF VARIOUS COMPOUNDS IN THE TISSUES AND ORGANS, FROM THE BLOOD.

The special changes produced in the blood as it circulates through the capillaries of the different organs will be referred to in their proper place, but it is desirable to consider at once the general phenomena of the process of nutrition as it occurs in the elementary tissues of the body.

Before any tissue can be nourished, certain of the soluble substances formed in the blood and held in solution in the serum, must permeate the walls of the vessels, and traverse the texture. The nutrient fluid having perhaps undergone some change in its eourse, reaehes the masses of germinal matter of the several textures, by whieh it, or eertain of its nutrient eonstituents are taken up. Thus the germinal matter increases by the formation of new germinal matter; and the loss of that which has already undergone conversion into tissue is to some extent, eompletely, or in eertain eases more than, eompensated for. These proeesses in the healthy eondition oeeur at a definite rate, but if the eapillary walls be unusually thin, or be stretehed, they neeessarily beeome more permeable to the fluids passing from the blood; or if the soluble nutrient matters be formed in the blood in undue proportion, a greater amount of pabulum must pass to the tissues than is suffieient to compensate for the waste occurring. Consequently, under such eireumstanees, the masses of germinal matter increase in size. If this exeessive proportion of soluble pabulum were not very soon taken up by the living germinal matter it would, at the temperature of the body, soon undergo decomposition, and the resulting products would, probably, very soon destroy all the living germinal matter in the neighbourhood, as well as the existing tissue. At the same time that the masses of germinal matter increase in size and number from inereased aeeess of pabulum, the tissue or formed material becomes softened and altered in eonsequenee of being too freely permeated by the fluid.

Changes affeeting the quantity and quality of the soluble nutrient substances in the blood, and their distribution to the tissues, frequently form the starting point of many morbid proeesses whieh, after proceeding for a eertain time, may eease, or be eaused to stop, or they may be compensated for by aetions of a different nature being exeited in other parts; or, running on to a eertain degree, the entire destruction of a tissue which eannot be renovated or replaeed, may result. If a eonsiderable extent of the tissue of some highly important organ as brain, lung, liver or kidney is affeeted, the patient's death may occur long before the ehanges have reached the degree to which they often attain when confined to a small cireumscribed

portion of comparatively unimportant tissue as skin, bone or connective tissue.

There can be little doubt that from the same pabulum different kinds of germinal matter produce substances having a very different chemical composition. Nor are we able to explain why one form of germinal matter should produce muscle, another fibrous tissue, another nerve, and so on. On the one hand there can be no doubt that all these different kinds of germinal matter have descended from one, and on the other it is probable that from them all a common form of germinal matter (pus) might result; while the germinal matter of muscle or nerve may cease to produce these higher kinds of formed material, and give rise to fibrous tissue alone. It would seem as if, by virtue of some original power, the germinal matter of the embryo evolved in due order the several kinds of germinal matter which, under conditions brought about at the proper time, give rise to the formation of their respective tissues, but that if, from altered conditions, the production of the series were interfered with, the formation of the special compounds and tissues became impossible in that particular organism. The changes would go on in order until the perfect organism was produced; but any interference or derangement of these would render the ultimate attainment of the perfect form in that particular case impossible.

The great importance of the nuclei, or masses of germinal matter of the tissues, in connection with each special formative process has been already indicated, and the conclusions arrived at render it very improbable that those which are constantly, and in such great number, met with in connection with the capillary vessels are unimportant, or are connected only with the development of the vessel as has been supposed. These masses of germinal matter, varying in size and number in different capillaries, and in the same vessels under varying circumstances, often project into the cavity of the vessel, and on the other hand extend beyond the line of its external wall. In inflammations and fevers these masses sometimes increase to four or five times their normal size.* Moreover, it is well known that fatty degeneration of these capillary nuclei, and

* Microscopical Researches on the Cattle Plague, a Report to Her Majesty's Commissioners, by Lionel S. Beale, M.B., F.R.S., &c. May, 1866. See also plate V, fig. 46, and plate VII, figs. 67 and 68.

other morbid changes, are associated with most important alterations in the character of the blood, and serious derangement in nutrition as well as in the actions of the tissues. It is, therefore, almost certain that these bodies are intimately concerned in the changes taking place in the blood and in the tissues in health. It seems not improbable that the masses of living or germinal matter under consideration are concerned in the selection and distribution of materials to the tissues as well as in the removal of substances from them and their introduction into the blood. When they project considerably into the interior of the vessel, the red blood corpuscles must, one after the other, come into contact with them, and probably part with some of the oxygen with which they are charged. This may combine with some of the elements just set free by changes in the living matter, and many of those chemical compounds which are obtained from the blood result. Under ordinary circumstances these bodies may take up nutrient matter from the blood into which they project, while on the side directed towards the tissues, the germinal matter may become resolved into substances fitted for the nutrition of the various textures.

Milk.—Some of the most important substances formed by the agency of special germinal matter from the fluid constituents of the blood are those which enter into the composition of milk. This secretion contains, without doubt, all the materials necessary for nutrition and tissue-formation—*albuminous*, *saccharine matters* and *earthy salts*, dissolved; and *fatty matters in a state of extremely minute subdivision*, suspended in fluid. All these different classes of substances are undoubtedly formed by the secreting cells of the mammary gland, and the pabulum of those secreting cells must be derived from the blood. The arrangement of the vessels, the disposition of their nuclei, and their relation to the secreting cells, differ in no essential respect from what is observed in other secreting organs, and there can be little doubt that the material distributed to the cells of the lacteal gland is a simple serous fluid, the elements of which are rearranged by the germinal matter, and caused at last to combine to form the peculiar substances characteristic of milk.

Casein.—This principle has many properties in common with albumen and fibrin. It is found abundantly in milk. Its occurrence in other fluids has not been positively determined.

The curd which is formed by heating milk in which a free acid existed, consists of a combination of casein with the acid. Heat alone will not effect the precipitation; but the addition of a little acid of any kind will occasion it. When dilute sulphuric acid is added to skimmed milk a precipitate occurs which is sulphate of casein. By digesting the clot thus formed with water and carbonate of lime, the acid combines with the lime, and the casein, which is set free, though not in a pure state, dissolves in the water and may be obtained by evaporation. It exists in the proportion of 3 to 4 per cent. in women's milk and in cow's milk, and 2 per cent. in asses' milk.

Casein is coagulated very perfectly by the action of rennet (the fourth or true digesting stomach of the calf) aided by heat. This property of coagulating casein is not to be attributed to the acid of the calf's stomach, but to the organic principle (pepsin) resident in it; for the power remains after all evidence of acid reaction has been removed. Rennet is one of the most powerful agents in causing the coagulation of casein, and it has been employed in domestic economy for the manufacture of cheese, which consists of the curd mixed with butter, compressed and dried. So perfect is its coagulating power that not a particle of casein in milk submitted to its action, will remain uncoagulated.

Casein comports itself with reagents in a manner very similar to albumen. In the coagulated state, it is insoluble in water, but soluble in *liquor potassæ*. It is not precipitated by heat alone, in which respect it differs from albumen. Casein, unlike albumen, is precipitated both by acetic and lactic acids.

The fatty matters present in milk, amount to about 4 parts in 100. They occur in the form of separate globules, each of which is protected by an envelope of casein, which prevents them from running together. Chevreul obtained from butter of cow's milk, the glyceride of stearic, palmitic, oleic, capric, caprylic, caproic, and butyric acids, but it is doubtful if these bodies exist in this state in the fresh secretion.

Sugar of milk ($C_{12}H_{24}O_{12}$) is a crystallisable substance existing in the proportion of about 4 parts in 100 of milk. In women's milk, the sugar varies from 3 to 6 per cent. In asses' milk it amounts to 4·5, and in mare's milk to 8·7 per cent. It is formed only in the secreting portion, and probably by the cells,

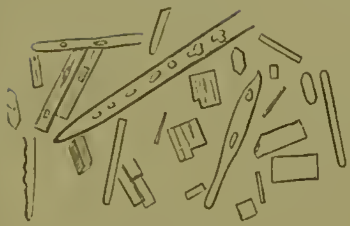
of the lacteal gland and does not exist in the blood. If cane sugar or grape sugar be injected into the blood of animals while suckling their young, these forms of sugar do not find their way into the milk, but milk sugar is formed as usual; while, if this latter substance be injected into the blood of an animal, it becomes converted into grape sugar, and is excreted as such in the urine.

The saline matters present in milk, consist of alkaline chlorides and phosphates, with potash and soda in combination with the casein, and phosphates of lime and magnesia, which are dissolved in company with this substance. The proportion of the different constituents of milk varies much under different circumstances and in certain acute diseases.

Fatty matters,—are to be obtained in greater or less proportion from almost all the fluids and solids of the animal body. They exist in three different states in animal bodies—1, *dissolved;* 2, in the form of *minute granules,* as in the chyle; and 3, in quantity, forming *large* or *small globules.* Pl. I, figs. 1 and 2. The production of fatty matter from germinal matter has been already alluded to (p. 103), and minute examination of the elementary parts of the various tissues seems to show that fatty matters may be formed under certain circumstances from any of them. It may be regarded as certain, that a perfectly transparent albuminous material may give rise to the formation of fat; it is well known that fatty acids are found among the products of decomposition of albuminous substances. Not only may germinal matter, which at one time was perfectly clear and transparent, develop oil globules, but fatty matter may be seen to appear in perfectly transparent and structureless germinal matter *after it has* been removed from *the body.* Careful microscopical observation will convince any one that the fatty matter of ordinary adipose tissue results from changes occurring in its germinal matter. Pl. III, fig. 33*a*, *b*, *c*. While, when the fat already formed is to be re-absorbed, it is probable that it is again taken up by the germinal matter, and its elements transferred to the germinal matter of the blood. In the case of adipose tissue which undergoes absorption rapidly, as the fat bodies of the abdominal cavity of the frog and newt, the masses of germinal matter of the fat vesicles and of the capillaries are large, and those of the latter numerous.

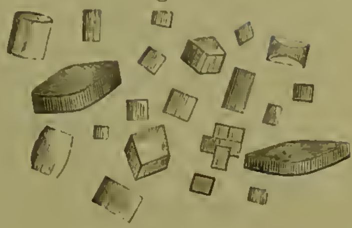
CRYSTALS. UREA. URIC ACID, &c.

Fig. 70.



Crystals of urea.

Fig. 71.



Crystals of uric acid.

Fig. 72.

Hippuric acid.

Fig. 73.

Epithelial cell. Air-cell of lung. Cattle plague. Myelin particles in outer part. × 1800.

Fig. 74.

Myelin particles from the external portion of cells in air-cells of the lungs. Cattle Plague. × 2800

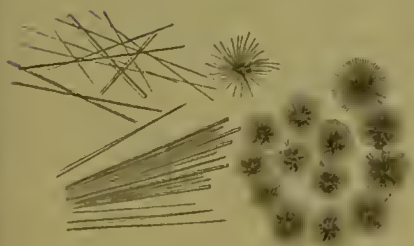
Fig. 75.

Taurin, after Funke

Fig. 77.

Cholestrine. *a*, from pneumonic lung. *b*, from fluid round an hydatid cyst. *c*, from the brain. × 215.

Fig. 76.



Crystals of Leucine, after Funke.

Fig. 78.

Myelin from the brain. × 215.

$\frac{1}{1000}$ of an Inch ____ × 215.

The saponifiable fats occurring in the organism of man are *Olein*, *Margarin*, or perhaps more correctly, *Palmitin*, and *Stearin*. Margarin is probably not a simple substance. Pl. VII, fig. 69. Margaric acid consists, according to Heintz, of a mere mixture of stearic and palmitic acids. The fatty acids are *Oleic acid* ($C_{18}H_{34}O_2$), *Stearic acid* ($C_{18}H_{36}O_2$), and *Palmitic acid* ($C_{16}H_{32}O_2$).

Cholesterin ($C_{26}H_{44}O$), Pl. VIII, fig. 77, and *Serolin*, are the only non-saponifiable fats found in the organism. They are very widely distributed and exist in large quantity in connection with all parts of the nervous system. They are also present in the bile; and cholesterin is not unfrequently met with almost pure in certain kinds of gall-stones. These non-saponifiable fats increase as the textures in which they are found advance in age. In young textures the proportion is much smaller than in the adult, and at an early period of development mere traces are to be detected in nerve tissues, which in their fully developed state yield a considerable proportion. Moreover, in many tissues in which at an early period, and even in a fully formed state, no cholesterin can be detected, this substance exists in considerable proportion in old age; and in certain diseases in which morbid changes induce, at a comparatively early period of life, alterations resembling those which occur under ordinary circumstances in advanced age, cholesterin is one of the substances resulting from the altered chemical changes.

Myelin.—It has been recently shown, by some very interesting researches of Beneke's, that the peculiar fatty matter termed myelin may be obtained from all the tissues of the body. In the liver it exists in large quantity; it is found in all parts of the nervous system; and much may be obtained from the yolk of egg. It is yielded even by albuminous matters and fibrin.

Myelin was first described by Virchow, who showed that it was not an ordinary fatty matter, as it swells up and is soluble in water. Its peculiar characters are well known. It is colourless, glistening, semifluid, prone to form drops, and capable of being drawn out into long threads, which curve and twist into the most peculiar forms. The masses often exhibit double contours, and not unfrequently many lines may be discerned equidistant from one another, but varying in their apparent thickness and intensity. Myelin is soluble in hot alcohol, ether,

and turpentine. It contains both nitrogen and phosphorus, like Fremy's cerebric and oleophosphoric acids. It yields the reaction characteristic of the biliary acids, with Pettenkofer's test.* Beneke obtained the reaction with the alcoholic extracts of almost all the tissues. Cholesterin is a necessary component of all forms of myelin, and it seems to be rendered soluble by the other constituent of this substance; indeed, Beneke has shown that myelin is in fact a mechanical mixture of *cholesterin* and *cholate* of *lipyl.* It would seem not improbable that, as Beneke suggests, the oxide of lipyl (the hypothetical body which yields glycerine on hydration) separated from the fatty acids by the action of the pancreatic juice, is presented in a nascent state to the biliary acids which then combine with it, forming a cholate of lipyl. This then becoming mechanically mixed with the cholesterin, myelin results. Myelin is represented in plate VIII, figs. 73, 74, and 78.

Muscle.—The germinal matter of both striped and unstriped (voluntary and involuntary) muscle produces contractile material, which consists principally of a substance termed syn-

* The following are Pettenkofer's directions: Pour a portion of the suspected fluid into a test tube and add English sulphuric acid, guttatim, to about $\frac{2}{3}$ the volume of the fluid, whereby the temperature is considerably raised. The addition must be made so gradually that the temperature shall at no time exceed 145° F., as otherwise the choleic acid is too much changed; then add 2—5 drops of ordinary cane sugar solution containing 1 part sugar to 4—5 parts of water, and shake the whole. If choleic acid be present, a more or less deep violet red colour will be produced according to the amount of bile in solution.

Neukomm (ueber die Nachweisung der Gallensäuren, &c., 1860,) proposes the following modification: "A single drop of a $\frac{1}{20}$ per cent. solution of choleic or glycocholic acid will yield a splendid purple violet colour if it is brought in contact with a drop of dilute sulphuric acid (4 water, 1 sulphuric acid) and a trace of sugar solution in a porcelain cup, and then gently warmed over a spirit lamp; as 1 cubic centimetre equals about 8 drops, it is thus possible to demonstrate $\frac{6}{100}$ milligr. of biliary acid with complete accuracy." As a further test he suggests "the biliary acid or salt is to be sprinkled with a small quantity of concentrated sulphuric acid moderately warmed and then water added. The resinous flocculi that subside are to be separated from the acid, washed with water, but not so as to remove all the sulphuric acid, and then again gently heated in a porcelain cup till coloration ensues. If the residue be taken up in a small quantity of alcohol, and the green solution be evaporated, the interior of the cup will be coated with a deep indigo blue film, even when but little acid has been used. If the biliary acids have been impure, or the sulphuric acid or the temperature react too long, the pigment film will be green." See the abstract of Beneke's Memoir "On the Occurrence, Diffusion, and Action of the constituents of the Bile in the Animal and Vegetable Organism," by Dr. Duffin, Archives of Medicine, vol. iv, p. 192, 1865.

tonin, or muscle fibrin. The contractile material is associated with a small quantity of delicate passive texture, moistened with fluid holding several different substances in solution. Syntonin, from σύντονος, contains in 100 parts, C 54·06, H 7·28, N 16·05, O 21·5, S 1·11. It resembles fibrin in many of its properties, but unlike this substance it is insoluble in a 6 per cent. solution of nitrate of potash. Kühne has obtained syntonin in a fluid state from striped muscle, and considers that this is its condition as long as contractility lasts, but that stiffening of muscle after death, or *rigor mortis*, is due to the coagulation of this substance. It dissolves readily in water containing $\frac{1}{1000}$ of hydrochloric acid. When the acid solution is neutralised the syntonin forms a jelly. Soon after death a free acid is formed in the juice of the muscular tissue, probably from changes in the syntonin. Du Bois Raymond showed that no free acid was to be detected in the muscles in a state of rest. Indeed, as long as the muscle retains the property of contractility it appears not to exhibit an acid reaction, but after it has lost this property, acid is rapidly developed. The amount of acid to be obtained from the juice of muscles after death is remarkable, and Liebig has calculated that the voluntary muscles alone contain more than sufficient to destroy the alkalinity of the blood (Lehmann).

The colour of the muscular tissue of animals with red flesh is an organic colouring matter. It is probably allied to hæmatin, and the intensity of the colour is increased by oxygen.

Among the chemical substances obtained from muscle, and probably resulting from disintegration consequent upon action, are the following: *Kreatine*, *Inosite*, and *Phosphoric*, *Lactic*, *Butyric*, and *Inosic acids.*

Kreatine ($C_4H_9N_3O_2$, H_2O) is a crystallisable substance, existing in the proportion, according to Gregory, of about five grains in one pound of flesh. The muscles of birds, probably from their much greater activity, contain about three times as much kreatine as those of fishes. Kreatinine ($C_4H_7N_3O$) is also found in the juice of muscle.

Inosite ($C_6H_{12}O_6$, 2 H_2O), or muscle sugar, is soluble in alcohol, from which it may be obtained in crystals resembling those of gypsum. According to Scherer it is isomeric in its anhydrous state with anhydrous grape sugar. This substance hitherto

has only been found in the muscular tissue of the heart in animals (Lehmann). Kidney-beans contain about 0·75 per cent., when unripe.

Inosic acid ($C_{10}H_{14}N_4O_{11}$?) is not crystalline, but forms crystallisable salts with the alkalies. *Phosphoric*, *Lactic*, and *Butyric acids*, obtained from the juice of flesh, have the same characters as those acids obtained from other animal fluids.

The *fatty matters* contain olein, palmitin and stearin, with oleo-phosphoric acid (Valenciennes and Frémy). The *ash of flesh* contains phosphate and sulphate of potash, chloride of potassium, earthy phosphates, and iron.

Nerve.—The nervous tissues consist principally of an albuminous substance combined with peculiar fatty materials, perhaps partially dissolved as soaps. The nerve cells contain more water and albuminous matter, but much less fatty matter, than the nerve fibres in connection with them, and at an early period of development the proportion of fatty matter present in the nervous system is very small. The tubular membrane, or nerve sheath, is composed of a substance nearly allied to elastic tissue in composition. It appears probable that the albumino-fatty material existing in such large proportion in the medullary sheath, or white substance of Schwann, accumulates as the nerve fibres advance towards their fully developed condition. This fatty substance seems to form a protective covering to the axis cylinder within, and probably acts as an insulator, by which currents passing along neighbouring axis cylinders are prevented from acting and reacting upon one another by induction. The fact that this fatty matter of the white substance is neither formed nor removed under the same circumstances as the fats of adipose tissue, would seem to show that its relation to the ordinary changes occurring in the body is of a very different kind from that of the ordinary fats. The axis cylinder of the nerve, which, like other textures, is formed from germinal matter, consists of a substance allied in its chemical properties to yellow elastic tissue. It seems a very passive kind of formed material, and at any rate in many instances resists the action of chemical reagents, which completely destroy many other tissues.

The nerve textures contain, besides ordinary albumen, modifications of albuminous matters, which are not precipitated

from their solutions by boiling. Von Bibra states that the brain fats consist of cerebric acid, a number of different fatty acids, and cholesterin.

Cerebrin is of neutral reaction, and soluble in boiling alcohol and ether. According to W. Müller it contains in 100 parts C 68·35, H 11·30, N 4·69, O 15·66. It is also found in the yolk of egg and in pus, and probably in the fat of blood serum (Gorup-Besanez).

Oleo-phosphoric acid was discovered by Frémy, and has been found in the brain, spinal cord, kidneys and liver.

Olein, stearin, oleic and stearic acids, in part combined with soda, potash, or lime, and cholesterin, are also present in the nervous tissue. The substance known as *myelin*, which exists in connexion with the nerves in very large quantity, has already been referred to (p. 148).

The chemical substances obtained from white fibrous tissue, cartilage and bone, have been briefly referred to in page 113. Yellow elastic tissue yields a substance which is very insoluble, not altered by prolonged boiling in water, quite insoluble in cold strong acetic acid, and scarcely affected by potash and soda. By digestion in sulphuric acid, *elasticin* yields leucine, and by the action of nitric acid, xanthoproteic acid is formed. Donders has arrived at the conclusion that all fully formed cell membranes are composed of a substance closely allied to yellow elastic tissue, which might be termed animal cellulose. At an early period, however, of the process of cell formation, no such substance exists in any cells, and in some, no cell-wall can be demonstrated at any period.

The epithelial textures, as epithelium, epidermis, various kinds of nail, horn, and hair, wool, whalebone, feathers and tortoise-shell, consist of a substance allied to the protein compounds and containing from 1 to 5 per cent. of sulphur. Associated with the protein compound, at an early period of life, is a certain proportion of amyloid (see page 111). The colouring matter formed in connection with epithelial textures is produced at the same time as the soft, horny material. It is an organic colouring matter, which, like other natural organic colouring matters, results from changes occurring in a perfectly colourless germinal matter.

THE CONVERSION OF PABULUM INTO BLOOD.

The simplest organisms obtain their pabulum from the medium which surrounds them. This seems to be at once absorbed into the organism, taken up by the germinal matter, and converted into the peculiar constituents of the body. But in more complex structures, the pabulum derived from without, is not already adapted for the nutrition of the tissues generally. It is, in the first instance, taken up by certain special masses of germinal matter which grow and multiply at its expense. The substances resulting from the death of these particles, consisting of compounds not to be detected in the original pabulum, are afterwards taken up by the germinal matter of the various tissues. Thus the spongioles of the plant probably absorb the crude materials from the soil in a state of solution. These are converted by the living matter into new substances, which circulate in channels, and are taken up by the germinal matter entering into the formation of the cells of the various tissues of the plant. In like manner, it appears that nutrient materials in their crude state, cannot be directly appropriated by the tissues of man, but must pass through several stages of preparation, undergoing conversion entirely into new substances which did not exist before, and which are peculiar to his organism alone. Even substances closely allied in composition to the tissues to be nourished, and in a state of solution, are not directly appropriated by the tissues; nor, if injected into the blood, would they be rendered by that fluid fit for this purpose. They must be first modified by various preliminary operations, taken up successively by two or three series of cells (masses of germinal matter), of course in a totally altered form, and not until then are compounds produced, which are adapted for the nutrition of the tissues. If either of these successive processes be modified by an altered action of the cells the pabulum is not properly prepared and the textures suffer in nutrition.

The new constituents, whether albuminous, starchy, saccharine, or fatty, which are to be added in the blood, to supply the place of the materials which are being removed from it in the process of nutrition, are probably taken up from the intestinal surface in a soluble form, and appropriated by germinal matter,—

entering into the composition of the chyle corpuscles which grow and multiply in the lacteal vessels, as well as the white blood corpuscles, circulating in the capillaries. At the same time that these masses of germinal matter are increasing in size, and giving rise by division to new masses, a certain proportion of the mass probably becomes resolved into the various soluble substances which enter into the composition of the serous fluid. All the new pabulum must, therefore, pass into the blood in these two forms, as masses of living germinal matter, varying in size, which become the white, and at length the red blood corpuscles, and *serum* which consists of a solution of albumen in water, with the so-called extractive matters, traces of fatty matter, and various kinds of salts.

There is reason to infer that very few alimentary substances can be taken up directly by germinal matter of the intestinal surface. Most of the materials entering into the composition of our food require most important preparation and undergo great modifications before they can be appropriated by any living matter at all. Thus, starch is converted into a form of sugar by the saliva and pancreatic fluids—fatty matter is rendered capable of absorption by the action of the latter secretion and the bile. Insoluble albuminous matters are rendered very soluble by the action of the gastric juice, and most important changes, which are as yet very imperfectly understood, are doubtless effected in the contents of the alimentary canal by these and the other secretions poured into it in such enormous quantity. The substances so prepared are appropriated by the germinal matter, and this appropriation mainly constitutes what has been termed *primary assimilation.*

The germinal matter of the tissues, as has been already explained, undergoes conversion into the tissue itself. This tissue is often greatly modified after its *formation.* It may undergo condensation by the removal of water and the approximation of its particles, or it may be rendered firm and hard by the deposition of calcareous or other salts in its substance or in its interstices, and these may chemically combine with it, or be merely deposited. The organic matrix of bone, teeth, and some other tissues is first formed by germinal matter, and the earthy material to which its physical properties are entirely due, is subsequently deposited. The *formation* of the

matrix itself is the result of a *vital* process, but the impregnation of this matter with saline matter is probably due to chemical changes alone.

We may, then, conclude that in the preparation of the substances required for the nutrition of the germinal matter of the different tissues, the lifeless pabulum, after being rendered soluble, is appropriated by the living matter of the cells of the villi. Portions of this germinal matter then die, and the products resulting from their death become taken up partly by the germinal matter in the lacteals, partly by that in the walls of the capillaries, and partly, perhaps, by the white blood corpuscles. These forms of germinal matter probably give rise to white blood corpuscles from which the red blood corpuscles are produced. By the action of oxygen upon these last, probably two series of compounds result; one which is capable of being appropriated by the germinal matter of the capillary walls and that of the tissues, while the other becomes resolved into carbonic acid, urea, and other compounds which are eliminated by particular organs of the body. From the nutrient matters so prepared the germinal matter of the various tissues derives the substances for its nutrition, and these, when taken up, become part of its substance, and take the place of that portion which has recently undergone conversion into tissue.

In the removal of old and worn out tissue and the introduction of its elements into the blood prior to their elimination by the various excreting organs, it is probable that similar operations occur, the old texture being taken up by germinal matter, this undergoing conversion into formed material, which is appropriated by the germinal matter of the vessels and the white blood corpuscles, until at last, by the disintegration of those substances which serve as pabulum to the secreting cells of various glands, imperfectly, or highly oxidised bodies, are prepared, which are at once carried off.

Alteration in composition of Formed Material in Disease.—The integrity of the formed material of many tissues is preserved, and the activity of its function maintained, by the continual passage of fluid through it. The disposition of the nuclei, or masses of living germinal matter in the healthy tissue, is such as to ensure the existence of currents through every part. If from a change in the composition of the fluid itself, or in consequence

of an alteration occurring in the masses of germinal matter, the tissue is no longer permeated, or permeated irregularly, by these currents of fluid, most important changes soon result. The products of decay not being carried off as fast as they are formed, and not being converted into readily soluble sub stances, accumulate, and seriously interfere with the action of the tissue already formed. Such is, in part perhaps, the explanation of the changes which occur in the formed material of various cells and elementary parts, which are said to be affected by degeneration.

The formed material of tissues is also sometimes modified in consequence of being bathed with fluids of composition different to that which obtains in the healthy state, and this alteration in composition may be due, in part, to the characters of the pabulum, and partly to the conditions under which its preparation is carried on, or as frequently happens, to the circumstance that certain excrementitious compounds, which ought to have been entirely eliminated, remain in the fluid.

The character of the formed material will also be influenced by the rate of its formation, and this will, to some extent, depend upon the amount of pabulum which reaches it, and which, of course, varies much in different cases.

In the preparation of this chapter, the Author as received much valuable help from his friend and colleague, Professor Bloxam.]

CHAPTER III.

OF TISSUE, ITS STRUCTURE AND PROPERTIES.—TISSUE PERMEABLE TO FLUIDS.—HARDNESS.—ELASTICITY.—FIBROUS STRUCTURE.—EPITHELIAL TISSUE.—CONTRACTILE TISSUE.—NERVOUS TISSUE.

ALTHOUGH the different tissues are apparently formed in the same manner, they vary remarkably in their structure, arrangement, composition, and properties. It is the special province of the histologist (ἵστος, tissue, web) to investigate the structure and arrangement of the various tissue elements. We shall not, however, restrict ourselves to this alone, but in the course of our enquiries into structure shall endeavour to learn something about the development and action of the texture; some observations upon structure have been already made in Chapter I, and upon page 70 will be found a tabular view of the tissues of the human body. We propose in this place to offer a few general remarks upon the properties and minute structure of tissues before we describe seriatim the individual characters of each.

It has been shown that all formed material was once in the state of germinal matter. The characters manifested by the formed material, or tissue, after it has been produced, are dependent, in great measure, upon the changes which occurred during the living state. So also must we refer the *structure* which the formed material exhibits, as well as its properties and chemical composition, to the changes which occurred when the matter was living, modified by the influence of external circumstances at the moment it passed into the formed condition. Nothing seems more ridiculous than to attribute the properties of tissues peculiar to things living to the properties of the lifeless elements entering into their composition—to refer elasticity, contractility, porosity, or other characteristic property to the properties of the oxygen, hydrogen, nitrogen, carbon, and of other elements of which the tissue is composed. To suggest that the addition of a little nitrogen or oxygen to a non-contractile mass might induce in it the property of contractility would be rightly considered, frivolous, and yet suggestions as absurd have been seriously advanced, if not

really entertained, by some who it would seem are determined to force the acceptance of the dogma that all the properties of things living are due to the properties of the elements entering into their composition, and to these only.

Tissue permeable to Fluids.— The tissues of living beings are in almost all cases traversed by fluid holding in solution certain matters which are to take part in nutrition or which result from disintegration. In this way the integrity of the texture is preserved, and gradual changes in it are effected. Even the hardest tissues are not absolutely dry or impervious to fluid, and there is reason to think that the intimate structure of tissues so hard as bone, dentine, and enamel is preserved by the continual passage of small quantities of fluid through it. In many soft and very moist tissues the very rapid circulation of fluid is continually going on, as may be proved by causing coloured fluids to traverse it. The natural fluid which passes to and fro in every part of the tissue through interstices too delicate to be seen, preserves it in a healthy state. If this process were to be suspended even for a short time, the tissue would suffer and in some cases be so damaged that it would no longer perform the function it was formed to discharge. In effecting the flow of these currents of fluid through the tissue the germinal matter is the active agent. And if a tissue be carefully examined it will be found that the position of the masses of germinal matter with respect to one another, and to the source from which the fluid is derived, is such that not a particle of the intervening tissue can escape being bathed with new fluid as it flows towards or from the vessels which supply fresh pabulum and carry off the deteriorated matter. In this way changes are continually provoked in every part of a solid tissue. There is no stagnation anywhere, and every particle is successively bathed with fresh portions of fluid. If from change in structure, or from the death of the germinal matter, stagnation does occur, the tissue soon suffers. It ceases to act, soon loses strength, and slowly degenerates, or is suddenly destroyed, in which case it is soon separated from the surrounding healthy parts, and is detached as a lifeless decomposing mass, capable of being appropriated only by the lowest forms of vegetable life, which grow and multiply at its expense if the germs are brought into contact with it.

In some instances the exact paths taken by the nutrient fluid as it flowed towards the living matter during life can be demonstrated in a tissue removed very soon after death. In the intervals between the converging lines which the fluid takes towards the centre of a cell, formed material has been deposited in such a manner as to give rise at last to a stellar arrangement of tubes which open into a central space originally occupied by germinal matter.—See fig. 28, plate III, p. 84.

Tissue, there is reason to think, is so constructed in some cases as to allow certain fluids only to traverse it and to prevent the passage of others. And it may be formed in such a way that fluid will permeate it in one direction only, or the internal structure may be such as to allow special fluids to traverse it in one direction, and solutions of another character in the opposite.

Hardness.—The property of hardness which is essential to certain textures is due either to the gradual desiccation of a soft protein formed material, or to the deposition in a soft matrix previously formed of mineral salts which undergo a modification and hardening in the tissue with which they sometimes seem to blend, if not to chemically combine, but the salts never assume in the substance of the tissue their ordinary crystalline forms.

Hair and horn and nail are examples of tissues of the first class. Of such textures the external hard coriaceous covering of insects, and some crustacea is as firm and hard and as serviceable for the firm attachment of muscles as bone itself. Bone which forms the basis of support for the soft parts in man and the higher animals, the dental tissues, the calcareous plates of the starfishes and echini, the external integument of some of the crustacea, and the shells of many mollusca are tissues of exceeding hardness in which this physical property is due to the impregnation of an organic matrix with hard calcareous salts. In some instances the firmness of the tissue is due to impregnation with silica, or some other mineral substance.

Elasticity.—Every kind of tissue, whether soft or hard, possesses the property of elasticity, so that it will return to its original bulk soon after it is released from moderate compression or stretching to which it may have been subjected. Some tissues are more remarkable for elasticity than others, but even the very softest and most fragile are elastic. This may be

shown by placing the tissue in a medium of much higher specific gravity than that which bathes it during life, when it will be found that although considerable shrinking may have at first taken place, the particles of the tissue by reason of their elasticity will gradually return to the positions they originally occupied. Thus the softest textures may be immersed in strong syrup or glycerine, which are highly efficient preservative media, without any reduction in volume if only we are careful to increase the density of the fluid by slow degrees, and allow time for the gradual expansion of the tissue after the reduction in volume which it has undergone in consequence of the osmose of the fluid from its interstices into the dense surrounding medium which of course ensued immediately it was introduced into the dense fluid. A knowledge of this fact is of the utmost importance to all engaged in microscopical researches upon the minute structure of the tissues.—See the method of preparing tissues given on page 57.

Some tissues are specially valuable for their elasticity, as for instance the different forms of elastic tissue, and it is very remarkable that as the fibres or laminæ of this tissue gradually increase by the deposition of new matter upon the outside, this last is so laid down that as it contracts and acquires consistency and firmness, its elasticity accords with that of the texture previously formed, so that there is no puckering or irregularity or unevenness to be observed in any part of the fibre, which however curls up a little on the side opposite to that on which the new tissue was last deposited. In connection with the vascular system elastic tissues play a highly important part, and the due performance of the respiratory act is dependent upon the elasticity of the pulmonary textures. Indeed, to such an extent is this the case, that if the structure of the elastic tissue of the lungs becomes impaired by disease, serious derangement of the respiratory function follows. The elastic membrane constituting the capillary wall not only permits the occurrence of great alterations in the internal pressure of the blood without the danger of rupture, but allows varying proportions of nutrient fluid to escape into the surrounding tissues. The minute quantity of fluid which permeates the capillary walls when these recoil upon a narrow quick moving stream, contrasts remarkably with the large proportion poured out when the capil-

laries are stretched to five or ten times their diameter, or distended to the utmost with scarcely moving or temporarily stagnant blood. Indeed to such an extent may the process of distension and engorgement be carried that longitudinal rents or fissures may result. Through these red blood corpuscles even, as well as the minute portions of living matter found in the liquor sanguinis, fig. 44, plate V, page 124, may freely pass. When, however, the distending force is withdrawn, the capillary, by reason of its elasticity, returns to its former diameter, and resumes its ordinary appearance of delicate homogeneous membrane, without an indication remaining of any rent or tear, or opening through which a very minute solid particle could make its way.

Fibrous Structure.—Fibres may be drawn out, as it were, from a mass of germinal matter in one, or in two or more directions, giving the mass of germinal matter an oval, spindle-shaped, or stellate form. *Thin structureless expansions* may be produced directly by germinal matter, or fibrous-like membranes may be formed, in which the fibres run parallel, or cross at various angles, giving rise at last to a tissue of such extraordinary complexity that it seems almost hopeless to endeavour to unravel it, and impossible to find out how fibres, running in so many different directions, were developed. By careful examination at different periods of the development of such a tissue, the observer will however, in some cases, be able to form as clear a conception concerning the manner in which the interlacing fibres were deposited, as he may gain of the mode of formation of a complex spider's web, by careful examination at short intervals during its formation, without having witnessed the creature actually at work. So delicate are the fibres in some tissues that they can only be detected by resorting to artificial colouring. Careful investigation leads us to think that in many cases in which a tissue appears perfectly homogeneous and structureless, it is really composed of excessively fine fibres, which cannot be clearly discerned by aid of the methods of investigation at our disposal. The peculiar characters and arrangement of some structures can be accounted for by the movements of the germinal matter during their formation, and conversely we may learn much concerning the movements of germinal matter by a minute and careful investigation of the elementary arrangements of the tissue which has been formed by it. In the for-

mation of the elastic cartilage of the epiglottis, and some other textures, it seems probable that each mass of germinal matter revolves while it forms delicate fibres, which accumulate, and at length appear to be arranged concentrically round the space in which it lies. The fibres, in this case, seem to be formed somewhat in the manner in which the caterpillar spins its cocoon, except that in the case of the tissue, the process is interrupted, while the last is a continuous operation. The attachment of the germinal matter to some of these fibres may be distinctly seen in the particular texture referred to, pl. XV, fig. 130. In connection with the ganglion cells of the sympathetic of the frog, one of us (L. S. B.) has described a very remarkable spiral arrangement of the nerve fibres, which can be readily explained by supposing movements of the germinal matter, while we believe in no other manner can the facts be satisfactorily accounted for. So also by the careful study of the arrangement of the twisting of nerve fibres in many tissues, we become convinced of the never-ceasing movement of the masses of germinal matter, not only during the formation and development of the fibres, but afterwards, during the adult period of life. In this way only can the highly intricate structural arrangements, familiar to us in many organs of man and the higher animals, be explained.

Changes, however, take place in many kinds of tissue after the formative act has been completed. In some cases the part which was first produced dries up, and gives rise to irregularities or cracks, which appear as peculiar markings, and may be characteristic of the fully formed structure. Sometimes a tissue, which for a long time appears homogeneous and clear, gradually acquires a fibrous appearance from the tendency of the old tissue to split, or cleave in certain directions, which will in fact be found to correspond to the lines in which new tissue was deposited at an early period of formation.

Epithelial Tissue.—One of the simplest forms of tissue found in man and animals, and perhaps that which is produced most easily and most quickly, is cuticular epithelium. Possessing elasticity, and considerable extensile property, performing the passive office of protecting more important textures beneath it, upon which it rests, and with which it is often connected, this tissue is readily replaced, if removed, and when injured is quickly and effectually repaired. Epithelial tissues exhibit,

however, remarkable differences in property in different situations. One may be dry and firm, hard and resisting, forming a sharp point or cutting edge, as in certain kinds of nail and horn; another may be supple and elastic, like the epidermis, or soft and moist, like the epithelial tissue of mucous membranes and internal passages, while some forms of epithelial tissue are semi-fluid, or more or less viscid, of the consistence of mucus.

In hardness and resisting power different forms of epithelium differ from one another as much as any one of them differs from other tissues. The student would scarcely believe that the soft, moist epithelium of a mucous membrane was in any way related to the hard dry tissue of which nail, horn, and hair consist, or to the hard calcified texture of shell, dentine, or enamel; but if he were to examine these textures at an early period of their development he would be convinced of their very close relationship, and would find that the formed material was produced in the same manner in all. It may be truly said that one thing can scarcely differ more from another than the soft, moist epithelium of a papilla of skin or mucous membrane does from the firm cuticular tissue of horn or hair, and yet under modified conditions the former may become so altered as to constitute a tissue which any one would admit was closely allied to the latter structures. The fibre-like cells constituting certain forms of hair, horn, and nail are very different from other forms of epithelial tissue, but, as is well known, well-developed horns are occasionally produced on the skin, and the horny material consists but of modified epidermis. The long drawn out cells or fibres of enamel and dentine are probably modified forms of epithelium, the formed organic matter of which has been gradually impregnated with calcareous particles.

Nor do epithelial textures differ from one another less remarkably in structure and physical properties than they do in function. The cell which secretes bile, or urine, or gastric juice would seem to be very far removed from the epithelial cell of the cuticle or of a mucous membrane, for the former are instrumental in the production of secretions possessing very peculiar properties and containing much water, while the last produces only the dry horny matter which accumulates, or a softer material which, however, by gradual drying may be

converted into the same sort of passive substanee. The relationship is however distinctly seen in disease, for there are eonditions under which seereting eells eease to produee their characteristie seeretions, shrivel up and waste, and are at last so ehanged that some of them might easily be mistaken for a very simple form of non-seeerning eell structure.

A gland folliele itself, with its included epithelium, is, in the first instanee, but a diverticulum from the duet; whieh duet is but an infleetion of the general surfaee. In the formation both of the duct and the gland folliele epithelium is instrumental. Young cells may grow in a direetion from the duct, and multiplying in number may produce a little collection like that seen in the gland follicle, or a long series may result, as in the formation of tubular glands. Eventually the permanent epithelium of the seereting part of the gland differs so mueh in form and aetion from that of the duet, that had we not watched the evolution of both we should not have been inelined to believe in their eommon origin.

At an early period of development no struetural differences can be diseerned between the formed material produeed by those masses of germinal matter on the surfaee which are to give rise to epithelial eells and that formed by those beneath which are to take part in the development of fibrous tissues, vessels, nerves, and museles. But gradually the soft mueus-like formed matter disappears, and *tissue* exhibiting peeuliar struetūre, and manifesting special properties is slowly formed by the germinal matter. This constitutes the *tissue* of the epithelial eell, or of the subjaeent textures, as the ease may be. It is the outermost layer of the simple masses of germinal matter of whieh the germ eonsists that takes part in the produetion of cutieular and allied tissues. The proeess, having commeneed, continues as long as life lasts, and the loss of old epithelial eells upon the surfaee is eompensated for by the production of new ones beneath. But a modified form of eutieular tissue may be produeed in another way altogether. Where the healing process proceeds over an extensive surfaee after the removal of a considerable portion of skin, new euticle is at last formed. The formation of new cuticular texture does not only spread gradually towards the centre of the spaee from the intact cuticle at the margin of the wound, but new points of eutiele formation are seen to originate

as little islands even in the central part. This cuticular tissue must be formed by masses of germinal matter which have descended from those of the subjacent connective tissue corpuscles, or from particles of germinal matter descended from white blood corpuscles, of which a large number are usually found upon the surface of a healing wound, having escaped with the serum of the blood through the thin walls of the subjacent capillaries.*

The fact of the very intimate connection between the epithelium and subjacent connective tissue which exists in some cases, and the gradual transition by which in other instances one tissue is seen to pass into the other, lends support to the view that the germinal matter of connective tissue, and probably that of many if not all other tissues may, under certain circumstances, produce a tissue closely allied to simple cuticular texture. Some observers have arrived at the conclusion that the epithelial and nervous tissues are continuous—that the finest ramifications of the nerve fibres pass into and are structurally connected with the formed material of the epithelial cell. This view will probably turn out to be erroneous, but it shall receive full consideration when the structure of nerve texture is described.

Contractile Tissue.—One of the most remarkable examples of peculiar structure familiar to us, and one which cannot be at all satisfactorily explained at present, is striped muscle. But we must not conclude that the transverse markings are essential to contractile tissues, for they are completely absent in the case of involuntary muscular fibre. While, on the other hand, there are certain kinds of fibrous tissue, destitute of contractility, which possess distinct transverse markings. Nor are the striæ of muscle seen at an early period of development. They do not make their appearance until *contraction* of the tissue has repeatedly occurred, but the fact of their great regularity and constant uniformity in the same species precludes the possibility of these markings being due merely to some accidental variation in the refractive power of the muscular tissue. It is certain they depend upon the occurrence of important structural changes while the contractile material is in a very soft plastic state. They may be due to the rate of formation of the contractile material and the rapidity of the successive actions of the nerve current

* "On the Germinal Matter of the Blood." Mic. Journal, 1863.

instrumental in exciting contraction: and the depth of the contracting portions indicated by the varying distances between the lines in different cases may be accounted for by the altered rate of performance of the operations above referred to.

Nerve Tissue.—It has been generally considered that the tissue of the nerve fibre was peculiar and that its function was in some manner determined by the peculiarity of its structure, or by its chemical composition. Such a view is, however, not supported by facts. For when we come to examine the axis cylinder which is undoubtedly the active and really essential part of the nerve, being that which is alone instrumental in transmitting the current, we find that this filament possesses an exceedingly simple structure, and, at least in some animals looks very like ordinary fibrous tissue. Indeed, if we were shown only a very small piece of an axis cylinder of a frog's nerve fibre, and some pieces of fibrous tissue of the same shape and size we should not be able with certainty to distinguish one from the other. Can the axis cylinder be regarded as anything more than a very elongated band composed of a texture closely allied to white fibrous tissue, but formed of perfectly parallel and continuous strata, not disposed as distinct fibres but nevertheless tearing in the longitudinal direction only? Anatomical observation would justify us in concluding that if it were possible to replace an axis cylinder by a long filament of ordinary fibrous tissue, we should find that this would conduct the nerve current as effectually as the ordinary axis cylinder itself. We doubt if the axis cylinder is capable of undergoing any remarkable changes in internal arrangement during nerve action, and consider that whatever those changes may be, they are of such a nature that they might occur in other forms of tissue. The peculiarity of the nervous system upon which all its characteristic phenomena depend, is probably not any remarkable arrangement in minute structure, but simply uninterrupted continuity of conducting tissue. Nor have we reason to think that the germinal matter of nerve grows or lives very differently from other forms of germinal matter. It receives its nutrient material from the same blood and is derived from the same masses of germinal matter which give origin to other forms. Considering the characters and arrangement of the germinal matter and its relation to the formed material in all tissues, it

is not unreasonable to conclude that currents, and, perhaps, of the same nature as those discharged by nerve organs, are set free. But perhaps the reason why these do not act in the same manner and cannot, indeed, be rendered evident, is this, that there is no continuous tissue along which the currents could be transmitted in definite directions and no peculiarly constructed apparatus adjacent to them which they could influence. It is probable that very slight differences in the molecular changes, which occur when living matter dies, determine the form or mode which the force then set free shall assume. Heat, light, electricity, or active movement being manifested according as the vital power operates upon the material particles of the germinal matter which are about to undergo change. But the nature of this action cannot be explained. It must be accepted as an ultimate fact, and the structure and the properties exhibited by tissue must in like manner be referred to the peculiar influence of vital power temporarily associated with the particles of living or germinal matter without the agency of which not any kind of tissue can be formed.

CHAPTER IV.

FIBROUS TISSUE.—SIMPLE FIBROUS CONNECTIVE.—OF CELLS AND INTERCELLULAR SUBSTANCE.—OF THE SO-CALLED TUBE SYSTEM OF CONNECTIVE TISSUE.—WANDERING CELLS IN CONNECTIVE TISSUE.—MUCOUS TISSUE OF UMBILICAL CORD.—VITREOUS HUMOUR OF THE EYE.—CORNEA.—WHITE FIBROUS TISSUE.—LIGAMENTS AND TENDONS.—VESSELS AND NERVES OF WHITE FIBROUS TISSUE.—REPARATION AND REPRODUCTION.—CERTAIN CHANGES OCCURRING IN DISEASE.—YELLOW ELASTIC TISSUE.—FORMATION.—AREOLAR TISSUE.—INCREASE OF CONNECTIVE TISSUE AS LIFE ADVANCES.

One of the simplest forms of tissue which is most widely distributed among other tissues of man, and the higher vertebrata appears under the microscope to consist entirely of delicate fibres passing from one point to another. It has been already stated that extremely delicate fibres may be formed by every kind of germinal matter, and that these result from its death. The substance known as fibrin consists of fibres which interlace in all directions and which have been probably formed from matter produced by the white blood corpuscles, p. 123. A white blood corpuscle, a mucus corpuscle, or other kind of germinal matter may move onwards, leaving behind it a trail of newly formed lifeless material consisting of a mucous-like mass of delicate fibres. See Figs. 79, 80, 81, plate IX.

Fibres of fibrin gradually acquire firmness by the closer approximation of the material of which they consist, and the gradual expression from its substance of more and more of the fluid existing in relation or combined with it at the time of its origin from the germinal matter. The gradual production of these fibres may be studied under the microscope during the coagulation of a drop of *liquor sanguinis*, plate V, p. 124, figs. 44, 45, 47.

The germ consists, at a very early period, of masses of germinal matter only, but soon a very delicately fibrous formed material makes its appearance, and in this very simple texture the formation of the new tissues from the germinal matter proceeds. In the development of muscle, nerve, and most other textures a delicately fibrillated matrix may be distinctly

demonstrated before any indications of the special tissue which is to be produced subsequently, can be found. And even in the fully formed perfect tissue the remains of this primary and very simple texture may be discerned.

When a wound in the substance of a tissue is repaired, fibrin is first formed from the outer part of the white blood corpuscles. The germinal matter embedded in the meshes of this newly formed web of temporary tissue then grows and multiplies, and at length masses are formed from which a firmer and more lasting fibrous tissue results. This is deposited in definite layers, and in a definite direction, while the old temporary fibrin having served its purpose is slowly absorbed. The changes referred to have been carefully studied in the fibrin deposited from the blood in the repair of a wounded artery. Some idea of the characters of the coagulum first formed, and the changes which take place in it afterwards may be gained by reference to figs. 82, 83, plate IX.*

SIMPLE FIBROUS CONNECTIVE.

This very delicate texture, the simplest of all the tissues, is very widely distributed in man and the higher animals. Indeed there is scarcely a part of the body in which traces of it cannot be discerned. From the circumstance of its existing between the more important structural elements of higher tissues, and connecting them to one another, as well as to other tissues, it has been termed *connective tissue*. It has been supposed that this texture was designed to give strength and support to more important tissues, but it must be obvious to any one who examines any of the organs in question, that the various structural elements afford the most efficient support to one another, and are not in need of a special supporting frame-work of any kind. It is indeed very remarkable that such a view should have been entertained, as it is well known that at the time when the more elaborate tissue elements are softest, and therefore most in need of support, that is at an early period of their development, scarcely a trace of this connective tissue is to be found, while on the other hand, when the textures have acquired considerable firmness, and possess resisting power of

* "On the repair of Arteries and Veins after injury," by Henry Lee and Lionel S. Beale. Medico-Chirurgical Transactions. Vol. L.

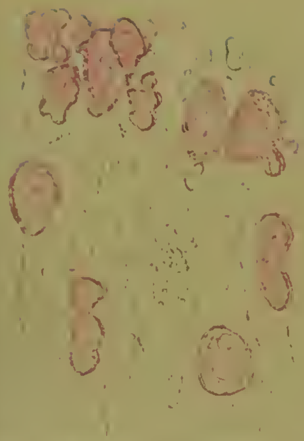
their own, this "supporting" connective tissue exists in very large quantity. The intervening connective, instead of being of advantage to the special elements of the tissue, actually interferes with their action, and its accumulation corresponds with the deterioration of the organ in which it takes place. Old texture differs from young in the greater proportion of its connective tissue, which results from changes occurring in the normal structure. And in many painful examples of chronic disease of important organs which come under the notice of the physician, the premature decay at a time when all parts of the body ought to be still in an active, vigorous state, is associated with abundance of connective, this being, in fact, the *débris* of the more important texture which has wasted. It is easy to understand how the connective tissue results during the development of textures in which the permanent type of structure is not manifested until several temporary textures have occupied the place of that which is destined at last to remain. These temporary textures gradually disappear, leaving a small quantity of what we call fibrous connective, and this collects, in most instances, at the outer part, because the formation of the new tissue takes place in a direction from within outwards. In studying the development of tissues, which consist of collections or bundles of fibres, as for example, muscular fibres, this point may be demonstrated very conclusively. The new fibres originate in the centre, and great differences in character between the outermost fibres, and those situated further inwards, will always be observed. From the first the masses of germinal matter, situated most externally, only produce connective tissue, and the muscle itself results from the development of those occupying a more central situation. The same fact is noticed in the development of nerve fibres. The masses of germinal matter, situated at the outer part of the bundle, do not produce true nerve fibres, but from them is formed connective tissue only. Up to a certain period the formation of true nerve fibres may have been possible, but a sufficient number of perfect fibres having been developed within, the marginal fibres degenerated, and took the low form of fibrous connective.

But the nature of this connective, and the mode of its production, are very conclusively determined by investigating the changes which occur during the development of a gland of highly complex structure like the kidney. The subject is so

important that it is worth while to consider the matter somewhat in detail. The *essential* structures in the fully formed kidney seem to be these—vessels for conveying the blood,—nerve fibres which govern the calibre, and thus determine the rate of flow of the blood from the arteries into the capillaries,—and epithelial cells which are arranged round the tubes so as to leave a channel by which the materials separated or formed by them may be readily carried away in solution in water. It is probable that these are the only anatomical elements which exist when the renal apparatus first begins to perform its active functions, and the only ones which constitute the simplest form of kidney. But as the growth of the body proceeds, the demand for a more extensive renal apparatus arises, and, as in the case of other organs in vertebrata, the increase must be gradual, and must take place while the organ is actively discharging its functions. The *growth* of the kidney necessitates a change in the relative position of the individual nerve fibres, vessels, and secreting structure in different parts of the gland, and the progressive development of new elements as extensions from those already existing. The successive changes are not easily traced with accuracy, and it is very difficult to convey in words a clear idea of the phenomena which succeed and as it were overlap one another.

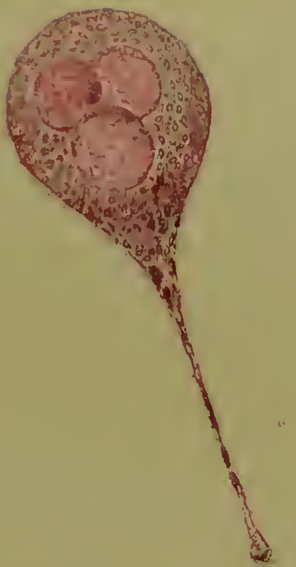
At an early period of development the secreting cells multiply and become arranged so as to form a hollow tube. By their division and subdivision the tube increases in length and circumference, at least during a certain period, in every part of its extent. At the deep or external portion of these cells, adjacent to the vessels, matter is slowly deposited in an insoluble form, and thus a thin membranous boundary which corresponds to the outer limit of the future uriniferous tube results, and this becomes extended as the cells grow, while at the same time it is increased in strength by the addition of new matter. Between the lines of masses of germinal matter from which the tubes are developed, and those which take part in the formation of vessels and nerves are a few masses which are not concerned in the formation of any definite structure, but which perhaps take part in the production of a small quantity of intervening substance. The membrane becomes further modified by its relation to the nerves and blood-vessels. These were very close to the cells at the earliest periods of development,

Fig. 7[illegible]



[illegible] magnified [illegible] p. 167

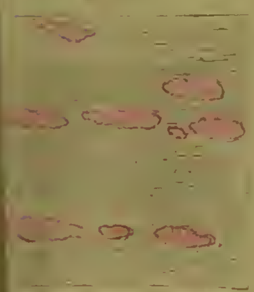
Fig. [illegible]



White [illegible] puscles (human subject), with a [illegible] fibrin (*a*) being formed from it. × 1500. p. 167.

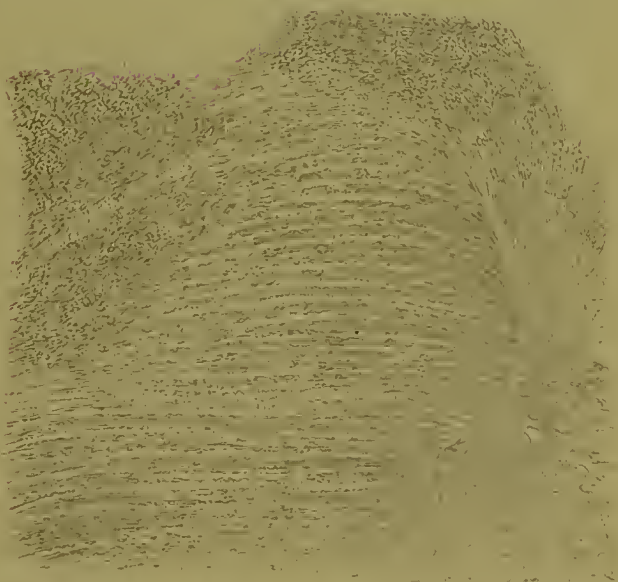
Fig. 80.

[illegible] in them. × [illegible] p. 167



[illegible]

Fig. [illegible]



Section through [illegible] of the [illegible] made in [illegible] occupied the wound and proceeded to [illegible] × 50. p. 168.

Fig. [illegible]

[illegible] p. [illegible]

[To face p. [illegible]]

and a very close relationship between them must be maintained throughout life or the free action of the gland would be impaired. Moreover, as the gland which already actively performs its functions grows, new nerve fibres and new capillaries must be developed around the uriniferous tubes. The position which a capillary or an ultimate nerve fibre occupies at an early period will at a later time be the situation where a bundle of nerve fibres, or small arteries and veins must be placed. The structural changes involved in all these alterations are considerable. Old capillaries and nerve fibres must be removed as new ones are developed to take their place, and all the original gland cells will have disappeared probably long before the uriniferous tubes have acquired their fully formed characters. But these structural elements are not *completely* removed. There will remain a small quantity of matter which cannot be taken up by the ordinary processes at work. This is no doubt capable of being removed like every texture in the body, but its complete removal would probably involve the destruction of the gland, while its almost complete removal permits of the continuous development of the latter and does not interfere with its continuous action. The conditions of existence in the case of man and the higher vertebrata, with a few unimportant exceptions only, permit the very gradual but not absolutely complete removal and renovation of tissues.

In insects, the state of things is very different, and in their textures there is an almost complete absence of connective tissue. The organs and tissues of the larva are entirely removed, while new organs and textures of the imago or perfect insect are laid down afresh and developed *ab initio*, instead of being built up upon those first formed. Such complete change, however, necessitates a state of existence during which action or function remains in complete abeyance. In the pupa or chrysalis period of life, functional activity is reduced to a minimum, and nothing is allowed to interfere with the developmental and formative processes. The new and more perfect being which is evolved does not probably retain a trace of the structure of its earlier and less perfect state. Although the elements of matter in the imago are, of course, those of which the larva and pupa were composed, they have been as completely re-arranged as they would have been had they been

introduced into the organism of another individual altogether. Not only have the old tissues been utterly destroyed and new ones produced, but in many instances these new ones belong to a totally different type; and were it not that observation has taught us that they have been really evolved at different periods during the life of one and the self-same individual being, we should have concluded not only that they belonged to different species, but in many cases to species far removed from one another.

In vertebrate animals there is not an organ in the adult but retains, not only the form which it assumed at a comparatively early period, but some of the very same tissue which was active in early life remains in an altered but deteriorated state. Every adult organ may be said to contain as it were the imperfect skeletons of organs which were active at an earlier period of life. This material which slowly accumulates, clogs and perhaps even in the most perfect state of things, slightly interferes with the free activity of the organ. If from any interference with the changes this unabsorbed debris accumulates in undue proportion the action of the organ may be very seriously impaired. It indeed soon grows old, while all the rest of the body may remain young. Its imperfect action deranges other processes of the body, and these react upon it until further action become impossible, and death results. The gradual but continuous and regular decay and renovation of an organ is normal in the vertebrate animal. The changes exhibit wonderful elasticity within certain limits, according to the demand for functional activity of the organ, but these limits, narrow in some, wide in others, cannot be exceeded without derangement and slow deterioration resulting.

This continuous renovation of an organ and accumulation of the skeleton of its earlier periods of existence may, however, be almost suddenly interrupted. In those changes which lead to the formation of pus the removal of every texture is as perfect as during the pupa state of the insect, but the germinal matter constituting the pus corpuscles has no power to give rise to that which will take part in the development of new tissues, while the germinal matter taking part in the removal of the larval tissues during the pupa state does possess this power, so that when in vertebrata this complete change occurs the organ is destroyed, and a new one is never developed in its stead. A part

of a complex organ may be destroyed and removed, but it cannot be formed anew, so that in man the gradual or sudden destruction of a great part of an organ necessary to life cannot be repaired, although in many cases the patient may adapt himself to the altered state of things and live under the changed conditions. The above considerations afford, I think, an explanation of the formation of the so-called interstitial indefinite connective found in greater or less amount in all organs of all vertebrate animals, and of its increase as age advances. The more regularly, gradually, and perfectly the changes are effected, the smaller will be the proportion formed, and the more slowly will it accumulate. When this is the state of things in all the organs of the body, health and longevity result. The opposite entails disease and too early death.

Of Cells and Intercellular Substance.—The connective tissues are supposed to form a class by themselves, and to consist of cells or cell forms embedded in an *intercellular substance;* and it has been held that the formation of the cells, and the production of the intercellular substance are distinct operations, although it has been proved that in this, as well as in all other textures, masses of germinal matter (the so-called cells) existed before any vestige of the intercellular substance was to be demonstrated. The connective tissues include the various forms of connective and fibrous tissues, cartilage, and bone. But the matrix of cartilage, as has been pointed out by one of us, is no more *intercellular* than the walls of epithelial cells. The relation of the so-called cells to one another, and to the cell wall, or intercellular substance in the two tissues respectively, will be at once understood if we call to mind the fact that the masses of germinal matter produce upon their surfaces the tissue, be it termed matrix, cell wall, or intercellular substance. This tissue accumulates between the masses of germinal matter. Even in epithelial textures, at an early period of formation, the formed material does exist as a continuous mass, which occupies the intervals between the several masses of germinal matter just as occurs in adult cartilage and fibrous tissue; but as growth advances, the portion of formed material belonging to each mass separates from its neighbours, and thus "cells" of epithelium result. The main difference, therefore, is at once perceived, for in the carti-

lage each "cell" is not marked off from its neighbours, but is represented by a mass of germinal matter, including a proportion of the so-called matrix, or intercellular substance around it. Some forms of cartilage are, however, really composed of "cells," which may be separated from one another just as in epithelium. The distinction, therefore, which has been drawn between different tissues, based upon the presence or absence of "cells" in the fully-formed texture, cannot be sustained.

Dark Fibres in Connective Tissue.—In every form of the simple fibrous connective tissue may be seen certain fibres, some sharp and well defined, others somewhat ragged and irregular, which are darker and more highly refracting than the rest.—Pl. IX, fig. 84. From the circumstance that the mass of the fibrous matter, of which fibrous tissue is composed, becomes perfectly transparent when treated with acetic acid, while these darker fibres are unaltered by this reagent, it has been

Fig. 85.

"Connective tissue from the embryo of a pig, after long-continued boiling," × 850. After Virchow.

inferred that two distinct textures exist in intimate relation with one another; the one being a gelatin-yielding substance, rendered perfectly transparent and structureless by acetic acid, the other allied to another form of fibrous tissue, the so-called yellow elastic tissue, which is not altered by this reagent. It has been maintained that the fibres exhibiting these different chemical reactions are formed separately,—that the gelatin-yielding fibrous tissue results from the "fibrillation" of an

intercellular substance, while the dark fibres, closely allied to yellow elastic tissue, are supposed to represent the cellular element of connective tissues.

In some of the plans adopted for the demonstration of the supposed cellular element most important textures would be completely destroyed. Thus in fig. 85, taken from Virchow, and representing the connective tissue from the embryo pig after *long-continued boiling*, and supposed to show the connective tissue corpuscles imbedded in their basis substance, most important textures, like nerves and blood-vessels, as well as the masses of germinal matter, taking part in the production of these, and of the white fibrous element, and of fat cells, and other structures, have been utterly destroyed by the process of preparing the tissue. It is unreasonable to suppose that anything can be learnt from examining the pulp of long boiled embryo skin, except the fact that of the many textures entering into its composition all are destroyed except the yellow elastic tissue. By such operations, as long-continued boiling, hardening in strong alcohol, drying, and the like, we cannot hope to gain anything but very erroneous ideas concerning the structure, arrangement, and offices of tissue elements.

Tube System of Connective Tissue.—Virchow has propounded the doctrine, that the fibres above referred to, and represented in fig. 85, which resist the action of acetic acid, constitute a

Fig. 86.

"Elastic networks and fibres from the subcutaneous tissue of the abdomen of a woman." After Virchow. a a "Large elastic bodies (cell bodies), with numerous anastomosing processes. *b b*, Dense elastic bands of fibres, on the border of larger meshes. *c c*, Moderately thick fibres, spirally coiled up at the end. *d d*, Finer elastic fibres at *e* with more minute spiral coils—300 diameters.

highly complex tubular system for the distribution of nutrient matter to every part of the fibrous intercellular connective sub-

stance—forgetting apparently that this could be more simply and more efficiently nourished by the free passage of the nutrient fluid everywhere through the interstices of the tissue itself, without the complex system of juice-conveying canals he has described. But thick walled tubes, composed of the least permeable of tissues, are hardly adapted for the operation. And when these tubes are to be demonstrated, the channel is found to be so very narrow that it is doubtful if the nutrient fluid would flow through it as fast as it would be required, if such a system of canals supplementing the blood-vessels was wanted at all; whilst it is quite certain that it would never permeate the enormously thick walls which it is admitted these canals possess.

But Virchow admits that these tubes gradually become impervious, and thus accounts for the fact that only very rarely can the tubular structure be demonstrated at all. He says, "it has not up to the present time positively been determined, whether in the course of this transformation, the condensation of the walls of the cells proceeds to such a pitch as entirely to obliterate their cavity, and thus completely destroy their powers of conduction, *or whether a* small cavity remains in their interior." *In transverse sections of fine elastic fibres it looks as if the latter were the case*, and there is therefore ground for *the supposition*, that in the transformation of the corpuscles of connective tissue into elastic fibres, nothing more than a *condensation* and *thickening*, and at the same time a chemical metamorphosis of the membrane takes place, but that ultimately, however, a *very small portion of the cell-cavity remains.** In short, it is admitted that the supposed nutrient tubes cease to be tubes, and cease to transmit nourishment at a time when nutrient plasma is still required, and may be demonstrated in the tissue itself, and at a time when the supply of capillaries is scanty; while at an early period of development, when the tissue is growing fast, there are no juice-conveying canals at all.

These supposed elastic tubular fibres consist of imperfectly formed connective tissue. Many are seen to be still connected,

* The theory necessitates the supposition that the cavity is obliterated by the deposition of matter in the interior of the supposed tube, but these yellow elastic fibres which are supposed to represent the cellular element and to constitute juice canals are certainly thickened by the deposition of new matter upon the surface. See "Yellow Elastic Tissue," page 203.

fig. 84, pl. IX, with germinal matter, and, as will be pointed out, the same fact is noticed in the case of the so-called nuclear fibres of ordinary tendon.—*See* p. 189. This *imperfectly formed fibrous tissue* refracts highly, and resists the action of acetic acid, while fully formed fibrous tissue is rendered transparent by it. The property of resisting the action of acetic acid does not, however, *prove* that a texture consists of elastic tissue, for, as is well known, nuclei generally resist the action of this reagent, which is so much employed in anatomical investigation for rendering the fully formed tissue transparent, and the nucleus, or mass of germinal or living matter, with the developing formed material around it, more distinctly visible.

Wandering Cells in Connective Tissue.—In connective tissue free masses of germinal have been detected, which have been observed to alter in form, and move like the white blood corpuscle, mucus corpuscle, and the germinal matter of the connective tissue itself. Recklinghausen, by whom they were first observed in the cornea, has given to these the name of wandering cells. In the tissues of the larvæ of the cold-blooded vertebrata such cells may be distinctly seen, and the alterations in form continue for some time, after the tissue in which they are present has been removed from the body. Various opinions have been expressed concerning their nature, but it will be remembered that one of us (L. Beale), in 1861, arrived at the conclusion, that all forms of germinal matter possess inherent powers of movement. The movements of the mucus corpuscles were minutely described, and soon afterwards (1863) the passage of particles through the capillary walls was referred to. These particles, detached from white blood corpuscles, were seen in the blood, and in the tissues external to the capillary vessels. The mode of formation of a thread of fibrin from a white blood corpuscle was watched, and the manner in which muscular tissue, white and yellow fibrous tissue, were formed, as the mass of germinal matter moved onwards was pointed out.

It is probable, that of the so-called wandering cells in connective tissue, some are descended from white blood corpuscles, others from lymph corpuscles, some from the germinal matter of the connective tissue itself. Many probably pass into the lymphatics and some into the capillaries; a few perhaps become transformed into fat. In certain forms of disease these free

masses of germinal matter divide and subdivide, and form collections which in some cases reach a considerable size. They may, there is every reason to think, even constitute tubercles or form the origin of tumours. In the majority of instances they no doubt degenerate, leaving in the situation they occupied granular matter, oil globules, and other matters which more or less interfere with the action of the tissue, which are often considered as resulting from changes in the tissue itself, instead of arising from this adventitious germinal matter, which has not perhaps originated in the tissue at all.

The phenomenon of movement occurs in all forms of germinal matter, and although it has not been demonstrated in every one, each year adds to the number of cases in which it has been actually seen. The view of tissue formation adopted by L. Beale involves the existence of capacity for movement in the germinal matter. These and other facts, now so much adverted to by many authors, afford very strong support to the doctrines advocated by him in the first part of this work, and in memoirs and books published previously.

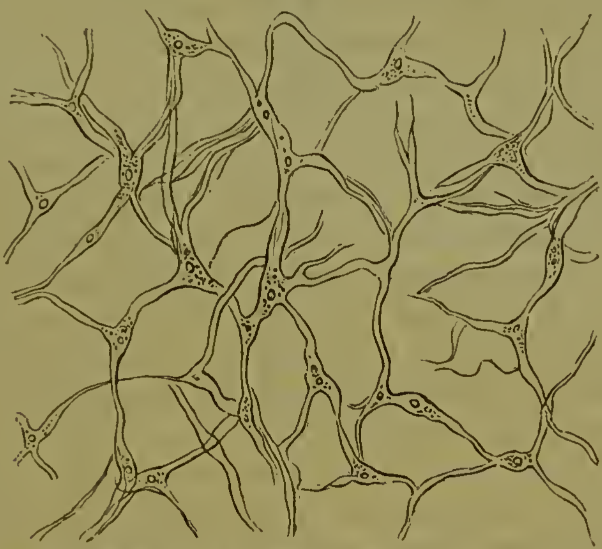
MUCOUS TISSUE OF THE UMBILICAL CORD.

Simple Fibrous Connective or Mucous Tissue of the Umbilical Cord.—One of the very simplest forms of fibrous tissue, and for this reason well worthy of attentive study, is the so-called mucous tissue of the umbilical cord, or the jelly of Wharton. The arteries and vein of the umbilical cord are connected together by a quantity of a soft form of connective tissue which corresponds in position to the connective tissue external to an ordinary artery. It serves to connect the arteries with the vein to form the cord. Virchow maintains that in this, as in other forms of connective tissue, special nutrient canals exist which freely anastomose with one another; and that thus is formed an extensive system of communicating tubes for the conveyance of nutrient materials to every part of this temporary texture, which is at every period of its life altogether destitute of capillary vessels. Virchow states that in a good preparation "a symmetrical network of cells is brought into view, which splits up the mass into such regular divisions that by means of the anastomoses which subsist between these cells throughout the

whole of the umbilical cord, a uniform distribution of the nutritive juices throughout the whole of its substance is in this instance also rendered possible."—*See* fig. 87, after Virchow.

We have, however, quite failed to discover anything like the arrangement Prof. Virchow has described. This "mucous tissue," according to our own observations, consists merely of a soft form of connective tissue, in which the fibres correspond exactly to the fibrous tissue (intercellular substance) of ordinary

Fig. 87.



"Transverse section of the mucous tissue of the umbilical cord, exhibiting the net-work formed by the stellate corpuscles, after the application of acetic acid and glycerine—300 diameters." After Virchow.

tendon. The fibres with the numerous nuclei are for the most part arranged to form the boundaries of more or less circular spaces.—Fig. 88, pl. X. In the spaces are seen more delicate fibres arranged without regularity, and the masses of germinal matter are much less numerous in the central part of the space than they are amongst the fibres which bound it, for it is in this latter situation that the formation of new fibres takes place. The germinal matter (nuclei) of the older fibres dies, and the fibrous matter itself is gradually altered and disintegrated—some few fibres, however, with some mucous-like matter, remaining in the central part of each space. The circular spaces are gradually increasing in diameter as the tissue advances in age, in consequence of the formation of new tissue at the circumference.

An *elementary part*, unit, or "cell," consists of an oval mass

of germinal matter, with ragged fibres projecting from either extremity, and often extending for some distance.—Fig. 89, pl. X. Many of the elementary parts are triangular, and the fibres pass off in three directions. The fibres have the general appearance of fibres of ordinary connective tissue, and the germinal matter extends for some distance in opposite directions, gradually tapering into a thin line, which is at length lost amongst the fibrous tissue. In the fresh tissue, therefore, there are no communicating tubes and spaces as have been described. The drawings in plate X, which are from actual specimens, do not at all resemble the diagrams Virchow has given of the same tissue. Compare fig. 87 with figs. 88, 89, pl. X. What is represented to be a space or cavity in the centre of the elementary parts is in the growing tissue, the precise situation of the germinal matter, as may be clearly proved by resorting to the method of preparation described in page 57. The apparent tubes contain prolongations from this. The soft germinal matter breaks down very soon after death, and in this way the spaces and tubes described may result, but it is certain that these do not exist as canals for conveying the nutrient juices during life. The nutrient matter instead of running in them permeates every part of the delicate fibrous tissue. The structure and mode of development of this fibrous tissue can be well demonstrated in specimens prepared according to the method given in page 57.

Some forms of the simple fibrous connective formed in disease are very like the simple connective tissue of the umbilical cord. Compare fig. 88, pl. X, with fig. 92. One of the fibres is shown separately in fig. 91, and it will be observed that the general structure and arrangement are the same as seen in the mucous tissue of the cord, and indeed in ordinary tendon and other forms of fibrous tissue. The great difference between the morbid and healthy fibrous connective tissue is to be observed as regards the formed material which is much more soft and yielding in the former, and in the arrangement of the germinal matter which is not so regular as in the normal tissue. But we may observe a gradual transition from ordinary fibrin with its germinal matter to the well marked and firm fibrous tissue of tendon and other fibrous textures.

VITREOUS HUMOUR OF THE EYE.

There is still much difference of opinion concerning the structure of this clear transparent tissue which contains more than 99 per cent. of water. Many years ago, one of us (W. Bowman) showed that in the infant at birth the vitreous humour was represented by a structure very much resembling the so-called enamel organ, and composed of elongated cells, with processes partly of a fibrous character radiating from them. Virchow regards the vitreous as an example of mucous tissue, like that just described in the umbilical cord, and considers that in the fully-developed vitreous humour the cells have disappeared, leaving only intercellular substance with mucus which he has detected in this structure. Kölliker agrees with us in thinking that at an early period the vitreous is composed of embryonic connective tissue. He considers however that subsequently, at least in its inner parts, every trace of this structure disappears, so that it comes to consist of a more or less consistent mucus. The structure of the vitreous and its mode of formation will be understood if fig. 90, pl. X, be referred to. This drawing is from the vitreous at an early period of its development.

The adult vitreous appears to be homogeneous, and not even the remains of cell structures or any indication of fibres can be detected in its substance. It is true that some observers have stated that even in the adult, cell structures were to be found in certain parts, and quite recently E. Neumann, of Königsberg, has convinced himself positively of the existence of cells in the vitreous of adult animals and man.

The vitreous closely resembles the transparent tissue which surrounds the ova of the frog and other batrachia. This tissue after having been dried swells up again almost to its original bulk when placed in water. Masses of germinal matter are to be seen in it at an early period of its formation; but when fully formed it seems to be composed of a very delicate tissue, probably the finest fibrous tissue that exists. It contains less than one per cent. of solid matter.

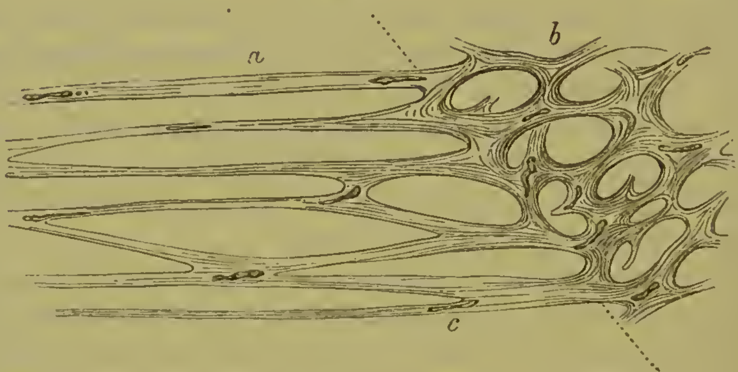
Upon the inner surface of the hyaloid membrane, which is continuous with the vitreous, round masses of germinal matter exist even in the adult. These are separated from one another

by pretty regular intervals, and from them a very soft tissue can be traced into the vitreous, of which it is, in fact, a part. The vitreous may therefore be regarded as a very delicate web, the fibres of which are combined with a considerable portion of water. The delicate fibrous tissue and fluid in its meshes bear to the masses of germinal matter the same relation as the formed material of other tissues bears to their germinal matter. The oldest part of the vitreous is that which is in the centre, while the circumferential portions were the last to be formed. The hyaloid membrane itself is probably but a highly condensed form of fibrous tissue of which the vitreous consists.

CORNEA.

The transparent proper tissue of the cornea is a modification of white fibrous tissue. It is composed of a number of branching fibrous fasciculi which are closely adapted to each other. These fasciculi are for the most part arranged in laminæ running parallel to the surface of the cornea. The fasciculi of one lamina are, however, continuous with those of adjacent laminæ. The arrangement of the bundles of fibrous tissue is such that a net-work is formed, the fibres of which are so closely adapted

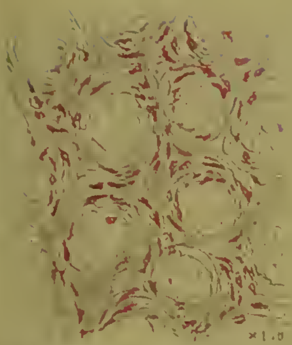
Fig. 93.



Vertical section of the sclerotic and cornea, showing the continuity of thin tissue between the dotted lines:—*a*. Cornea; *b*. Sclerotic; *c*. Masses of germinal matter or nuclei rendered more plain by the action of acetic acid.—× 820.

to each other that in the healthy cornea, intervening spaces can hardly be said to exist. The general arrangement of the fibrous tissue of the cornea and sclerotic is represented in fig. 93. Amongst the fibrous tissue of the cornea are situated the so-called radiating *connective tissue corpuscles*, or nucleated

Fig. [illegible]



[illegible] connective tissue [illegible] of the [illegible] the oval masses [illegible] with fibrous tissue [illegible] for a power of 130 [illegible] this figure with [illegible] 87, p. 17[illegible]

Fig. 9[illegible]

[illegible] us humour, with [illegible] matter. Human eye; [illegible] x 215. p 18.

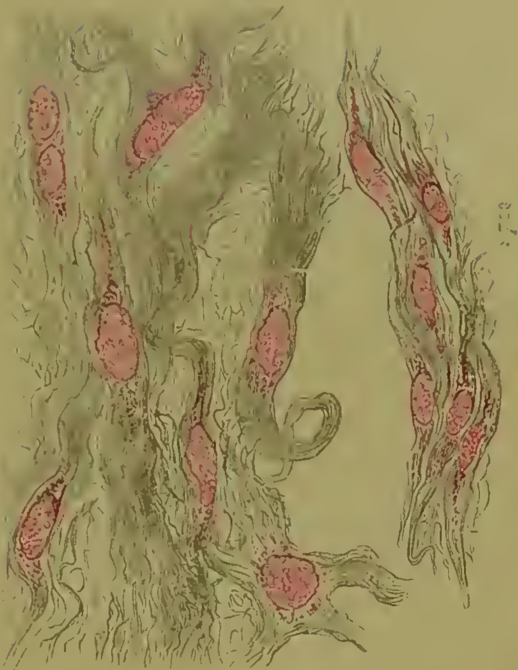
Fig. 91.

[illegible] part. [illegible] specimen [illegible] diameters. p 180.

Fig. [illegible]

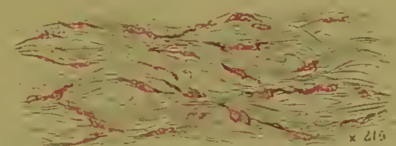
[illegible] muscle. Horizontal section. Rabbit [illegible] p [illegible]

Fig. 89.



A portion of the preparation represented in Fig. 88, magnified 700 diameters. The relation of the germinal matter to the formed material seems to be the same as in other forms of fibrous tissue. The "anastomosing nutrient tubes," described by Virchow, and represented in Fig. 87, p. 179, were not to be seen in this specimen. p. 180.

Fig. 92.



Thick false membrane found between the liver and diaphragm in a case of recent peritonitis, showing the germinal matter and formed material of this rapidly produced low form of fibrous tissue. X 215. p. 1[illegible]

Fig. 94.*

[illegible] Cornea [illegible] p. [illegible]

[To face p. [illegible]]

cells of the cornea. These were discovered by Mr. Toynbee in 1841. They have since been looked upon as peculiar to undeveloped elastic tissue, and, like those already considered, are supposed to be connected with channels for conveying the nutrient juices. Even Kölliker, who nevertheless maintains that white fibrous tissue is developed from cells, considers these cells or nuclei to be distinct from the fibrous tissue, and accepts Virchow's explanation of their office. He remarks:—"It is probably beyond doubt, that the nutrient fluid, which continually saturates the cornea in large quantity, is chiefly conducted and distributed further into the interior by the cells in question." If this be so, the nutrient fluids must be circulating in channels which lie between the fibrous bundles that are to be nourished. On this supposition it is not easy to explain by what process the fluid is made to pass into the innermost parts of the bundles, and by what forces constant interchange of fluid is effected.

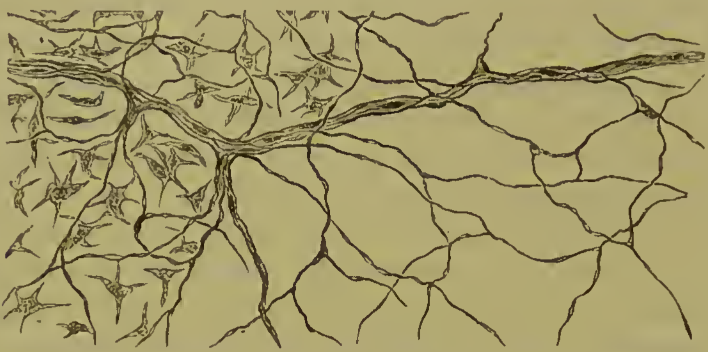
These so-called radiating cells, the branches of which anastomose freely with one another, are the masses of germinal matter of the cornea. They are directly concerned in the formation of the proper fibrous tissue of the cornea, and are much more numerous in a given bulk of young, than of fully developed tissue. The arrangement of these bodies is shown in fig. 94 and in fig. 94*, pl. X. *The fluids attracted towards these masses of germinal matter pass through the substance of the fibrous bundles*, and thus the integrity of the tissue is preserved. They have nothing in common with yellow elastic tissue, except that, like this tissue, they resist the action of acetic acid. See observations on page 177.

In the adult corneal tissue fluid may be forced into the spaces in which the germinal matter and its prolongations are situated, and may be forced from these between the lamellated fibres. In this way the "corneal tubes," which can be readily injected with mercury, are produced.*

* The corneal tubes may be injected in the cornea of the ox by proceeding as follows: after the muscles and their attachments have been carefully dissected from the globe, the epithelium and remains of the conjunctiva are to be scraped from the corneal surface, the eye being held firmly in the hand and pressed moderately. A large needle or sharp pointed knife may now be introduced into the corneal tissue at the side, and carried a little way into its substance and then horizontally for about a

It is doubtful if any actual tubes or cavities exist in the cornea during life, but by the arrangement above indicated, the corneal tissue is rendered much more permeable to fluids than ordinary fibrous tissue is.

Fig. 94.



Corneal corpuscles, and nerve fibres; Cornea of the green tree frog. The former are seen to be unconnected with the nerve fibres. × 350.

The nerves ramify in the proper substance of the cornea amongst the ramifications of their cells, but are not connected with them. The relation of the germinal matter of the corneal corpuscles to the nerve fibres is represented in fig. 94.

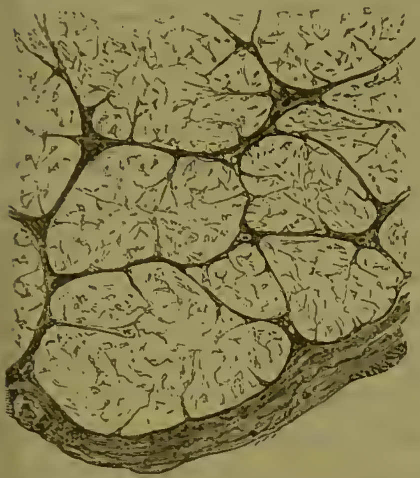
WHITE FIBROUS TISSUE.

Tendons, ligaments, and fasciæ, owe their firmness and unyielding properties to the white fibrous tissue of which they are composed. This white fibrous tissue is very widely distributed, but it differs materially in character in different parts. The three structures above named are all composed of white fibrous tissue, having well-marked characters. Cylindrical bundles, consisting of finer fibres varying somewhat in diameter, are bound together with indefinite or simple fibrous connective tissue, to constitute

quarter of an inch, so as to enter the lamellated tissue, care being taken not to perforate the cornea. A small globule of mercury may now be introduced into the channel which has been made, with the aid of a glass tube drawn off to a capillary orifice. A knife is to be applied to the aperture of the wound made in the cornea in such a way as to prevent the escape of the globule of mercury which at the same time is to be firmly pressed into the corneal tissue. It soon spreads and may then be made to pass to every part of the cornea. Some other forms of fibrous tissue may be injected by the same plan, but the spaces filled are not so regularly arranged as those in the cornea.

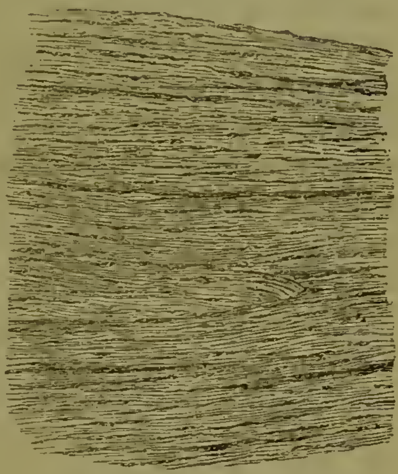
the tendon, ligament, or fascia. The few vessels and nerves distributed to this tissue, pass amongst these bundles, which in ligaments and tendons run parallel to one another, so that in a

Fig. 95.



Transverse section of tendon, showing bundles of fibrous tissue divided transversely with vessels and nerves in the intervals. × 30.

Fig. 96.



Longitudinal section of tendon. Bundles divided longitudinally to show direction of fibrillated structure. × 30.

transverse section different parcels are seen packed together, with the vessels and nerves in the slight intervals between them—figs. 95, 96. In fascia, the bundles cross one another at different angles and form flattened bands.

Physical Properties.—White fibrous tissue is *inelastic*, and, under ordinary circumstances, *inextensible;* though it does admit of being somewhat stretched by the influence of long-continued and slowly-acting force, as is seen occasionally when an effusion of fluid has taken place into an articular cavity, protected by a firm, fibrous capsular ligament, or where a tumour has slowly grown under a fascia. Its force of cohesion is the most valuable and characteristic quality of the white fibrous tissue, and to this its various important uses are chiefly due. Mascagni calculates the force requisite to rupture the tendo Achillis as equal to 1,000 pounds' weight. Instances are constantly seen where muscles are torn or bones fractured, while the tendons or ligaments, through which the force has acted, have escaped; thus the malleoli are often dragged off by twists of the foot acting on those processes of bone through the lateral ligaments of the joint. It is entirely devoid of contractility or irritability; and its sensibility is very low, so much so that tendons hanging

out of a wound have been cut without the patient being aware of it.

The flexibility of fibrous tissue is owing to its containing a small proportion of water. A tendon, ligament, or fibrous membrane, will dry readily; it then becomes hard and rigid; it resists the putrefactive process when not kept moist, and even then putrefies less readily than the softer textures. Acetic acid causes it to swell up, instantly removes its peculiar appearance of wavy fibres, and displays the remains of the masses of germinal matter concerned in its development. Gelatine may be extracted in considerable quantity from white fibrous tissue by boiling.

Of the different Forms of White Fibrous Tissue.—A. *Ligaments.*—Ligaments are connected with joints. They pass in determinate directions from one bone to another, and serve to limit certain movements of the joint, while they permit others. They therefore, constitute an extremely important part of the articular mechanism in preserving the integrity of the joint in its various movements.—There are three principal kinds of articular ligaments:—1. *Funicular*, rounded cords of white fibrous tissue, of which we may give as examples the external lateral ligament of the knee-joint, the perpendicular ligament of the ankle-joint, &c.: 2. *Fascicular*, flattened bands, more or less expanded; ex. internal lateral ligament of the knee-joint, lateral ligaments of the elbow-joint, anterior and posterior ligaments of the wrist-joint, and, indeed, the great majority of ligaments in the body: 3. *Capsular;* these are barrel-shaped expansions, attached by their extremities around the margin of the articular surfaces composing the joint, and forming a complete but a loose investment to it. The capsular ligament is highly developed in the enarthrodial or ball-and-socket joint, and permits the very free movements required. Good examples are found in the only two perfect examples of that form of articulation, namely, the shoulder and hip joints.

B. *Tendons.*—Tendons serve to attach muscle to bone, or some other part of the sclerous system. We may enumerate three varieties of tendon, as regards form:—1. *Funicular*, *e.g.* long tendon of the biceps cubiti; 2. *Fascicular*, short tendon of the same muscle, and most of the tendons of the body; 3. *Aponeurotic*, tendinous expansions, sometimes of considerable extent,

and very useful in proteeting the walls of eavities. The tendons of the abdominal muscles afford good examples of this variety.

The tendons are for the most part implanted by separate faseieles into distinet depressions in the bones, and are also closely ineorporated with the periosteum ; so that in maeeration, when the latter is separated, it beeomes easy to remove the tendons. In some birds whose tendons are black, the periosteum is black also ; and in the human subjeet we may often see the tendinous fibres continued on the surfaee of the periosteum, as a shining silvery layer, following the primitive direction of the tendinous fibres, from which they were derived ; a marked example of this may be seen on the sternum in front of whieh the tendinous fibres of the opposite pectoral muscles meet and deeussate, and thus form the superficial layer of the periosteum eovering that bone. The length of the tendons is beautifully adapted to the quantity of eontraetile fibre required to perform a eertain movement ; thus, in the bieeps cubiti, were the whole length between the seapula and radius oeeupied by museular fibre, there would be a great waste of that contraetile tissue, as there would be much more than is wanted to produee the required motion ; tendon is, therefore, made to take the plaee of the superfluous musele : in this way we may explain the differenees in length of the tendons even in the same limb.

C. *Membranous.*—In the form of an expanded membrane white fibrous tissue is used to eover, proteet, and support various parts. Under such eireumstances we often find that it not only forms an external eovering to them, but that it sends in processes or septa, whieh separate eertain subdivisions or smaller parts. Thus, the faseia lata of the thigh not only invests the museles of the thigh, but sends in proeesses whieh pass down to the periosteum, and separate the several museles from eaeh other ; and the dura mater of the eranium sends in proeesses by which eertain portions of the eneephalon are separated from one another.

Structure of Tendon.—When the areolar tissue has been disseeted off, the surfaee of the fibrous tissue exhibits a beautiful silvery white aspeet, and seems composed of bundles of fibres, whieh in some are arranged parallel to eaeh other ; in others are disposed on different planes and interlaee or eross in

different directions. On placing a very thin piece of the fibrous tissue under a high power of the microscope, we observe what may be considered the characteristic feature of this texture.

The piece under examination, fig. 97, pl. XI., seems to be composed of a leash of exceedingly delicate fibrillæ, running parallel to one another, and if not stretched, disposed to take a wavy course, like a skein of silk. But, on more accurate inspection, it is found impossible to distinguish threads of a determinate size; these seem, indeed, to be of various sizes according to the degree of splitting to which the whole has been submitted, and many are to be seen so very minute as at first almost to elude the eye. In other parts the mass splits up into membranous rather than filiform fragments; so that it would appear incorrect to describe this tissue as a bundle of threads. It is rather a mass with longitudinal parallel streaks (many of which are creasings), and which has a tendency to slit up almost *ad infinitum* in the longitudinal direction. The correctness of this view is further shown by the action of acetic acid, which obliterates, for the most part, all appearance of fibrillæ, and causes it to swell up as an entire mass. But the ordinary fibrillated structure reappears if the acid be carefully neutralized.

Tendon is generally subjected to examination after having been dried, or partially dried, and then remoistened with fluid, but it has been found that these processes cannot be carried out without some considerable alteration in the characters of the tissue being produced. With the exception of fig. 97, in which the germinal matter is not shown, the specimens represented in plate XI have been prepared without any desiccation at all. They have been soaked in carmine solution, and afterwards mounted in glycerine, according to the method already described in page 60. If a thin longitudinal section of tendon be examined, numerous narrow elongated bodies connected together by narrower lines, and arranged parallel to each other, and nearly equidistant, will be observed throughout the fibrous substance of the tendon. These are the "nucleated fibres of the tendon," or the parallel nucleated fibres, the *kern-fasern* of the German writers.—Figs. 98 to 102, pl. XI. The parallel, wavy, and delicately fibrillated matter between them is the white fibrous tissue of the tendon, the so-called *matrix* or *intercellular substance*, which is considered to be formed independently of, and

not to be connected with, the nuclei. The proportion which the "nuclear fibres" bears to the fibrous substance is different at different periods of development. If we examine the tendon of a fœtus, that from a young individual, and one from an adult of the same species, we shall find that the "nuclear fibres" are nearer together in the fœtus than in the young animal, and closer together in the latter than in the adult. In other words, as the tendon grows, the fibrous tissue or intercellular substance increases in proportion to the nuclear fibres; or in a given bulk of tendon, the nuclear fibres are much more numerous in embryonic tissue than in the same amount of that of the adult.—Fig. 101, *a*, *b*, pl. XI.

If the tendon be stretched longitudinally, the nuclei become narrower and appear as mere lines.—Fig. 100, *c*, *d*, *e*. On the other hand, if the structure be stretched laterally, the mass of germinal matter assumes an oval form, and the extension may be carried so far as to cause the masses to be wider from side to side than from end to end.—Fig. 100, *f*, pl. XI. The germinal matter thus extended forms but an exceedingly thin layer. The circumference is not so darkly coloured as the central part. Passing in a longitudinal direction are a number of lines (or rather the particles of which the germinal matter is composed, exhibit a linear arrangement) which run parallel with the fibres of the tendon, and these lines in the germinal matter may be seen, if a very high power be used, to be continued into the tendon, as imperfectly formed tendinous tissue.—Fig. 84, pl. IX, page 170. The direction of the fibres of the tendon is indicated by the arrangement of the particles of the germinal matter. These points which are of importance with reference to the nature of the so-called "nuclear fibres" can be demonstrated very distinctly in specimens of tendon which have been prepared in the manner described, and afterwards subjected to stretching and pressure without being previously dried.

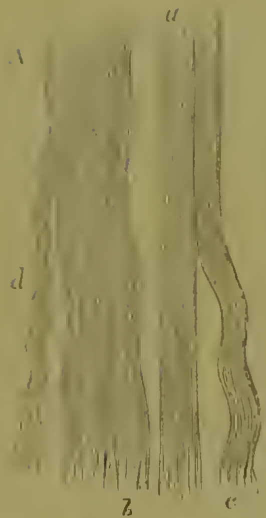
The appearances just referred to lead to the inference that the "nuclei" are continuous in all cases with the fibrous tissue of the tendon, and this may be positively proved to be the case in certain specimens, for the "nucleus" may be separated with fibrous tissue still connected with it.—Figs. 89, 91, pl. X, page 182; figs. 98, 99, 100, pl. XI. The fibrous tissue (intercellular substance) nearest to the nuclei or masses of germinal matter, is that

which was most recently formed; while that which is most distant is the oldest portion of the tendinous structure. Continuous with the particles of germinal matter is imperfectly formed fibrous tissue. As the germinal matter is exceedingly soft, and undergoes changes soon after death, and is destroyed by the action of water, it is not surprising that the continuity between the germinal matter and the firm fibrous tissue of the tendon should not have been generally recognized; but if care be taken to colour and harden the germinal matter, this continuity is made out very readily in every kind of fibrous tissue. If tendon well prepared be carefully torn up with needles, very delicate bundles may be separated; and it is not uncommon to find the oval masses of germinal matter with portions of white fibrous tissue projecting from either extremity.

From the fact that these oval bodies are coloured by carmine like the germinal matter of other tissues, and the fibrous tissue of the tendon is in direct continuity with them, we cannot but conclude that they are the masses of *germinal matter of the tendon, and bear the same relation to the fibrous tissue that the germinal matter bears to the formed material of other tissues.*

That this view is correct will be admitted, if allied tissues prepared in precisely the same manner be submitted to examination. As is well known, white fibrous tissue is in many cases immediately continuous with cartilage and bone. The matrix or intercellular substance of all these tissues is continuous, and if a section be made at the point where the fibrous tissue of tendon joins the cartilage or bone, one tissue can be traced into the other. The fibrous appearance of the first will be seen to gradually give place to the almost homogeneous or slightly granular tissue characteristic of the last. In fig. 129, pl. XV, page 230, is represented a very thin section through the tendo Achillis and os calcis (in that part which yet remains cartilaginous) of a kitten soon after birth. As the cartilage grows the masses of germinal matter divide, and the two portions at once separate from one another. In the tendon, however, the two masses resulting from division remain connected together by a thin line of germinal matter. Between the cartilage and the tendon is a layer which eventually becomes the *periosteum*. The stellate character of the masses of germinal matter in this situation is very distinct (under *b* in the drawing).

Fig. 97.



[illegible] fibrous tissue. *a* straight appearance of the tissue when stretched. *b c d* various wavy appearances [illegible] the tissue exhibits when not [illegible]. Magnified 300 diameters. T[illegible] B[illegible] 1843 p[illegible]

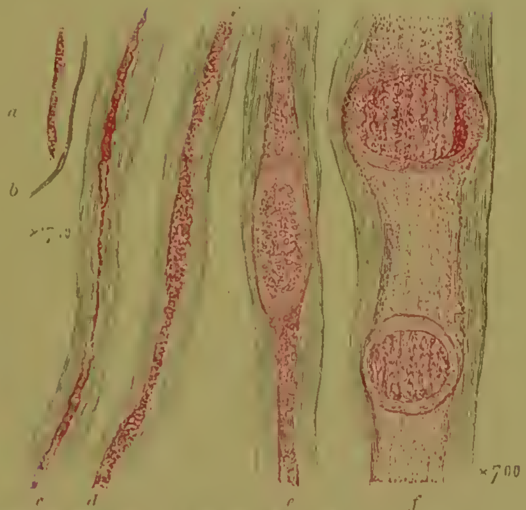
Fig. 98.

[illegible]ndo achillis. Kitten at birth. Showing the "nuclear fibres," consisting of oval masses of germinal matter, with narrow intervening portions, which have been described as consisting of yellow elastic tissue. ×700 p. 188.

Fig. 99.

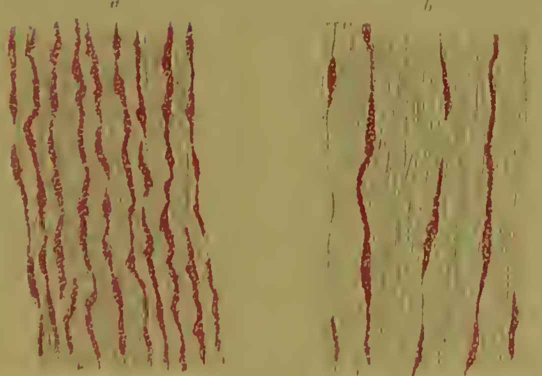
[illegible] fibrous tissue [illegible] [illegible]a, frog. Showing germinal matter and formed material. ×700 pp. 188, 191.

Fig. 100.



[illegible] Showing different appearances produced in the oval [illegible] germinal matter [illegible] in different directions. *a* appearance of prolongation of germinal matter [illegible] 700 diameters. *b* appearance of fine [illegible] of yellow [illegible] power. *c* [illegible] longitudinal direction. *d* [illegible] *e* [illegible] laterally. *f* appearance produced when the fibre [illegible] and subjected to pressure. ×700 p. 189.

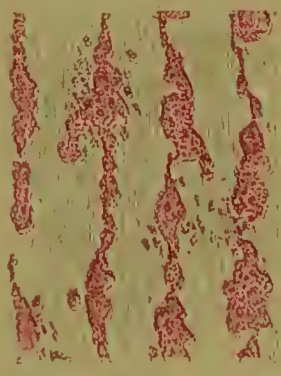
Fig. 101.



[illegible] × [illegible] ×

[illegible] development

Fig. 102.



[illegible] × [illegible]

A very different interpretation of these appearances has, however, been given by some authorities. The masses of germinal matter in tendon and allied tissues have been regarded by Virchow as connective tissue corpuscles, "bindegewebskörperchen," and he states that they are connected together by tubes. In a longitudinal section he admits that nothing like the stellate arrangement, seen in a thin transverse section, is observable. If an attempt is made to cut a transverse section of tendon, the stellate bodies are undoubtedly seen, but it is impossible to obtain a very *thin transverse section* of tendon with these in their natural position. In trying to do so, short pieces of tendon and the included nuclei are removed, with their prolongations of germinal matter and imperfectly developed formed material which resists the action of acetic acid, and being altered in relative position by the pressure to which the specimen is subjected, appear like stellate cells or corpuscles with radiating processes. In properly prepared specimens, however, the continuity of structure between the nuclei or masses of germinal matter, imperfectly developed formed material, and fully formed fibrous tissue, can be demonstrated.

In some specimens of young tendon these prolongations from the masses of germinal matter (*cells* or *nuclei*) are well seen, and their communications are tolerably numerous. The processes are distinct enough in some places, but most of them gradually become lost among the wavy fibres with which all are connected, and of which they are but the early stage. Although they somewhat resemble fibres of yellow elastic tissue in their general appearance and in their power of resisting the action of acetic acid, they are not of this nature; their outline is irregular, and when examined with very high powers they have a granular appearance, which is very different from the sharp outline and homogeneous appearance of true yellow elastic tissue.

Moreover, it must, too, be borne in mind that the appearance so remarkably distinct in certain specimens is not constant. It is not seen in a specimen of adult tendon where fibres of yellow elastic tissue are found, nor in that of a kitten; and in the fascia of the frog, fig. 99, pl. XI, there is no more indication of such an arrangement than there is in cartilage. In some specimens of the tendon of the child which have been stretched and

pressed, the appearance of *stellate cells and communicating tubes is* most distinct, but that it depends upon an alteration produced in the germinal matter, and upon the displacement and tearing away of some of the young tissue connected with them is sufficiently proved,—by the appearance in question being produced by pressure, by its absence in parts of the specimen not subjected to pressure, by the great variation of the appearance when it is seen, and by its entire absence in certain specimens.

The oval nuclei and intervening lines may be regarded as *spaces* and *tubes* in tendon some time after death, but in living tendon, and in tendon shortly after its removal from the dead body, the oval nuclei are composed of *living germinal matter* which extends from one to the other in the form of a very narrow line. Some time after death this germinal matter becomes broken down, and *there remain oval spaces and narrow tubes containing fluid and the products of disintegration of the germinal matter.*

Encircling Fibres.—Encircling the bundles of some forms of white fibrous tissue are to be seen, more especially after treatment by acetic acid, sharply defined fibres like those of yellow elastic tissue.—Fig. 104, pl. XII. It has been too hastily assumed that these elastic fibres are in connexion with the so-called nuclei and nuclear fibres (germinal matter) in the substance of the tissue. The existence of these fibres is undoubted, but they are not in sufficient number to be considered as essential constituents of the tissue, nor are they to be detected in all forms of white fibrous tissue. They wind round the bundles. By great patience we may occasionally succeed in finding a mass of germinal matter connected with some of these fibres, but when this is so, it is very small, and quite distinct from the masses amongst the white fibrous tissue. The delicate fibres of which the yellow elastic tissue is composed form a lax network on the surface of the bundles of white fibrous tissue. This is well seen in fig. 104, pl. XII.

But what is the nature of these encircling fibres of yellow elastic tissue which do not penetrate into the substance of the fibrous bundles? If the tendon of man, or any small animal be examined while development is going on, the vessels of which have been well and carefully injected according to the direc-

tions given in page 62, the true explanation will, we think, at once occur to the observer, who will probably be much surprised at the great vascularity of the texture. He will find numerous capillary vessels arranged around the fibrous bundles, as in the case of the elementary fibres of muscle. As the tendon gradually becomes fully developed, these vessels waste, and, as it seems to us, the delicate encircling fibres which have been described by so many authors alone remain to mark the channels in which blood once freely circulated.*

Sketch of the Changes occuring during the Development of Tendon and Allied Tissues.—Regarding the oval nuclei as the masses of germinal matter, and the fibrous structure which is in all cases connected with these, as the formed material, it is not difficult to account for the actual appearances observed in the different forms of fibrous tissue. At an early period of development these tissues like all others are composed almost entirely of germinal matter. The small masses increase, divide and subdivide in the soft imperfectly developed formed material which exists between them at this early period. In some tissues the masses of germinal matter soon become quite detached and entirely separated from each other, in which case the tissue will consist of formed material with the separate masses of germinal matter embedded in it, as cartilage. In others the masses of germinal matter divide in one particular direction, and separation of the resulting masses occurs laterally, while longitudinally they still remain intimately connected with one another. As the tissue advances in age, and the masses of germinal matter become separated from each other by gradually increasing distances, the formed material accumulates in parallel layers between the oval masses of germinal matter. These are connected by distinct lines of germinal matter and imperfectly developed formed material, and laterally, by finer and less obvious lines produced in the same manner. In those cases in

* I have demonstrated in very many tissues the fact that fibres having the reaction of yellow elastic fibres result from the wasting of vessels and fine nerve fibres. In the bladder and mesentery of a starved frog, the process of degeneration may be actually observed step by step, and in the serous pericardium and peritoneum of a very young mammalian animal positive evidence of a similar change may be obtained. The capillaries gradually transmit less and less blood, and as they contract in diameter the walls become more distinct. Slowly the cavity becomes completely obliterated and an apparently solid cord of elastic tissue alone remains.—(L. S. B.)

which the expansion of the tissue takes place equally in all directions, or equally in length, breadth, and depth, and the masses of germinal matter do not become detached, the tissue will consist of a matrix in which stellate masses of germinal matter are embedded. The radiating processes gradually become finer and finer as the tissue advances in age, until at last they quite disappear or leave narrow lines of imperfectly formed tissue which differs in chemical characters from that external to it, and resists the action of acetic acid like yellow elastic tissue. In tissues which are fundamentally composed of white fibrous tissue the most different appearances may be produced, according to the directions in which the structure expands, the rapidity of its growth, and the influence of stretching or pressure. In the various forms of fibrous tissue in the human organism, wide differences are observed, but in some of the corresponding tissues of the lower animals the differences are so great, that if only their anatomical characters in the fully developed state were studied, one would hardly suppose they were fibrous tissue at all.

Vessels.—White fibrous tissue when fully formed probably undergoes little change. It contains few vessels, but is nevertheless more vascular than is generally supposed. The majority of the capillaries of tendon under ordinary circumstances only transmit *liquor sanguinis*, with a very few blood corpuscles, and many appear as mere solid threads, and under ordinary circumstances no blood passes through them. If, however, the tissue becomes inflamed, the blood-vessels are obvious enough, and the tissue in this condition would be regarded as highly vascular. The alteration, however, is due, not to the rapid development of new vessels, but only to the passage of blood through many which before transmitted none. While tendon is undergoing development, it is highly vascular, indeed the vessels appear to be as numerous as they are in many other tissues. As development advances, many being no longer required, shrivel, and as has been already explained, delicate lines of elastic tissue remain in the situations in which they once ramified.

Many forms of fibrous tissue are almost destitute of vessels in the adult state, undergo scarcely any change, and require for their nutrition a very small quantity of nutrient pabulum.

Nerves.—It is generally stated that white fibrous tissue is destitute of nerves, but in every form numerous nerves which, however, form meshes of considerable diameter are to be detected. In the dura mater, in the perichondrium of cartilage, and the periosteum of bone, in the cornea, and some other fibrous textures, nerves are exceedingly numerous, and perform important offices. In tendon, however, the greater number of the delicate nerve fibres present are those which belong to the capillary vessels, to the small arteries, and to the veins. The first are often seen in considerable number, and not unfrequently a delicate fibre is observed running on either side of the capillary vessel, connected with one another by transverse branches at short intervals.

Reparation and Reproduction.—When a solution of continuity takes place in white fibrous tissue, it readily heals by the interposition of a new substance, every way similar to the original tissue, excepting that it wants its peculiar glistening aspect, and is softer, more bulky, and transparent.* In this process the changes are analogous to those described in page 193. When the tendon is divided, the cut ends separate, and the space between them is occupied by blood and lymph. This contracts somewhat, and thus the divided ends of the tendon are to some extent drawn towards one another. In the coagulum, thus formed, numerous masses of germinal matter are formed, which separate from one another, while soft formed material is produced by them. This gradually undergoes condensation, and at last assumes the characters of ordinary tendon. The changes which take place during the formation of this new tendinous tissue resemble in all important particulars those which occur in the development of the tendon itself at an early period of life—so simple is this texture, that it may in fact be *developed* at any period of life, and in almost any part of the body.

Certain changes occurring in White Fibrous Tissue in Disease.—In health the normal changes occurring in fibrous tissues seem to consist of the gradual increase in the quantity of the fibrous formed material, and the condensation of that which has been already produced. The fibrous tissues of the adult and of aged persons contain a higher percentage of solid matter than those of the child.

* We ascertained this in a case of a divided tendo Achilles.—T. & B. 1843.

The changes above referred to occur very slowly, and it is probable that very slight, if any, absolute disintegration and complete removal of white and yellow fibrous tissue takes place during life in the healthy state. These tissues are supplied with a very small proportion of nutrient matter, and the germinal matter is very slowly converted into fibrous tissue. But the fibrous material to retain its healthy state must be permeated in every part by fluids, which slowly pass to and from the masses of germinal matter. In certain cases, fatty matters are precipitated from the fluids amongst the fibrous tissue, or result from the degeneration of the imperfectly developed formed material around the masses of germinal matter, and in consequence the tissue deteriorates. In the low form of soft fibrous tissue in the umbilical cord, and in the placenta, this change invariably occurs towards the termination of the period of gestation. Very numerous oil globules and pigment granules are deposited amongst the fibres and precipitated amongst the particles of germinal matter. No such appearances are observed in the early months of pregnancy when the formation of tissue is actively taking place. In the higher forms of fibrous tissue corresponding changes are observed in advanced age—changes which are so constant that we are almost entitled to consider them as occurring normally; but in persons of healthy and vigorous constitution they are postponed to a much later period of life than in those whose nutrient processes have been impaired by disease and modified by the altered composition of the nutrient fluid. We have many opportunities of observing such a change in the case of the cornea. We have observed the arcus senilis wide and distinct in a man of forty years of age, while in the cornea of an old lady of upwards of ninety-eight the change had only just commenced.

Whether these changes result from the power of the germinal or living matter being impaired, or from an alteration in the composition of the fluids which are transmitted to it, cannot be discussed here; Mr. Edwin Canton has shown that corresponding changes occur in many other tissues of the body. That such tissue changes do not in all cases lead to fatal results is no more than would be expected, but this does not in any measure diminish their significance. Arcus senilis never occurs at the age of forty in strong constitutions, and it is very seldom

fully developed in persons who have lived very carefully, or who have weak stomachs and are dyspeptic, and have therefore been compelled to be careful, at the age of fifty or sixty.

Of Suppuration and Sloughing.—When the vitality of the nuclei of fibrous textures is destroyed, either from their not being supplied with nutrient matter, or in consequence of being bathed with fluid of an abnormal nature, the fibrous tissue becomes softened, and undergoes decomposition, and the dead portion is detached—in fact, sloughing takes place. If the germinal matter (nuclei, connective tissue corpuscles) be supplied with an increased quantity of nutrient matter, owing to the formed material, fibrous tissue, being rendered more permeable or otherwise modified, there is at first a tendency to the formation of new elementary parts (germinal matter and connective tissue), but if the change once commenced increases, the germinal matter multiplies so rapidly that no formed material is produced.—Fig. 102, pl. XI., p. 190. There is not time for the formation of any fibrous tissue whatever—in truth, the process of suppuration becomes established. Those soft connective tissues which contain the greatest number of nuclei (masses of germinal matter), and are most freely supplied with blood-vessels, and receive a large proportion of nutrient matter, are most liable to suppuration. The process of suppuration is, on the other hand, often arrested by a living fibrous tissue, as tendon or fascia. This fibrous tissue, resisting the tendency of the pus corpuscles to grow at its expense, retains its vitality, while softer and more succulent textures are destroyed.

YELLOW ELASTIC TISSUE..

Yellow elastic tissue differs from the white fibrous element in anatomical characters as well as in physical and chemical properties. Of a yellowish colour, very flexible, generally composed of fibres varying much in diameter, it is eminently elastic, and it retains its elastic power after removal from the body. In man it exists in the *fascicular*, *funicular*, and *membranous* forms, and is often disposed in bundles of fibres covered by a thin sheath of areolar tissue, which likewise sinks in among its fibres. This tissue may be preserved for many years in preservative fluids without its important physical property

of elasticity being in any way impaired. The action of this tissue is often antagonized by muscles, and the delicate movements of the ponderous head of the ruminant are effected by the contraction of the flexor muscles of the neck, which overcome the elevating action of the elastic ligamentum nuchæ.

In the following situations true yellow elastic tissue is found with well-marked characters: *Ligamentum nuchæ: ligamenta subflava: chordæ vocales:* many ligaments about the larynx. The *internal lateral ligament of the lower jaw*, the *stylo-hyoid* ligament, and the *transversalis fascia* of the abdomen, are also, in a great measure, composed of it. The *suspensory ligament* of the *penis* also consists of this tissue, and a modified form is found in the *elastic coat of arteries*, in the *trachea* and *bronchial tubes* and *pulmonary tissue.* Fibres of elastic tissue occur in connection with the *subcutaneous*, *submucous*, and *subserous* areolar tissue; and fibres generally considered to be of the same nature exist in connection with tendon and almost all forms of white fibrous tissue. Among the lower animals it is very extensively used for mechanical purposes as a soft elastic pad or buffer, or as strong elastic cords like the retracting ligament of the claw of feline animals, and the *ligamentum nuchæ* of quadrupeds. The true elastic tissue is in every case connected with, and developed from, nuclei (bioplasts), but there are many fibres, ordinarily regarded as yellow elastic fibres, which are but the remains of tissues (nerves and vessels) which were active at an earlier period of life. *See* page 214.

Although elasticity is the property which is universally characteristic of yellow elastic tissue, this structure does not exhibit an anatomical arrangement which is constant. As there are many different forms of white fibrous tissue distinguished from each other by the arrangement and general characters of the texture, and by the manner in which it was produced, so also we find a diversity in structure, arrangement, and mode of production of the *elastic tissues.* Under the microscope ordinary elastic tissue is found to consist of fibres, which are round in some, flattened in other specimens. These fibres are very variable in diameter, usually from $\frac{1}{5000}$ to $\frac{1}{100000}$ of an inch in diameter. In one bundle there are fibres varying much in age, the youngest as a scarcely visible line, the oldest of considerable thickness. The fibres bifurcate, or even divide into three; and

the sum of the diameter of the branches considerably exceeds the diameter of the trunk. Filaments of elastic tissue anastomose freely with each other. They are prone to break under manipulation, and the broken extremities are abrupt and disposed to curl up.—Fig. 107, pl. XII.; when many of these broken ends exist together in the same piece, they give it a very peculiar and characteristic appearance, which renders it almost impossible to mistake this tissue. The parallel fibres of the ligamentum nuchæ, figs. 107, 108, pl. XII., of the vocal cords, of the ligamenta subflava, and other pure elastic ligaments, differ widely from the lax network of long fine fibres of elastic tissue present in the areolar tissue beneath the skin and mucous

FIG. 109.

Finely fibrous layer of the longitudinal tissue of the aorta of the horse. × 200.

FIG. 110.

Coarsely fibrous layer of the longitudinal fibrous tissue of the aorta of the horse. ×200.

membranes, fig. 115, p. 205, among muscular fibres, connected with nerve fibres, &c. Both these forms are totally unlike the thin delicate longitudinal fibrous layer which lies just beneath the epithelium of an artery, fig. 109, and this again differs in important characters from the elastic tissue beneath, fig. 110.

The circular fibrous coat of the larger arteries contains a number of very coarse fibres, and in this situation is often seen

FIG. 111.

A portion of the circular fibrous tissue of the aorta of the horse, to show the reticulation formed by the interlacement of its fibres. × 200.

FIG. 112.

A portion of the circular fibrous coat of an artery, showing the penniform branching of the large rods of elastic fibrous tissue, each large rod giving origin to multitudes of small interlacing fibres. × 200.

a form of tissue which can scarcely be termed fibrous. The elastic structure seems to form a very coarse network which is

often spread out in a membranous form with numerous spaces or holes in it, figs. 111, 112.

Mr. Quekett found that the large fibres of the ligamentum nuchæ of the giraffe, exhibited transverse markings equidistant from each other, almost like striped muscle. These marks are not to be seen in all the fibres, and they are most distinct in the oldest. They do not extend quite across the fibre, but appear to arise from a shrinking of the central part, which causes it to break up transversely into smaller segments, fig. 113.

Fig. 113.

Large fibres of elastic tissue, with well-developed transverse markings. Ligamentum nuchæ. Giraffe. ×130.

Fig. 114.

Flakes from a large artery found in the stools, scarcely altered by digestion.—Natural size. *See* figs. 105, 106, pl. XII.

It is remarkable that fibres of elastic tissue from the sheep and ox, which have passed through the alimentary canal, without having undergone digestion, should sometimes exhibit transverse markings as distinct as those ordinarily observed in the fibres of the *ligamentum nuchæ* of the giraffe. In fig. 114 some flakes of yellow elastic tissue from an artery of a sheep or pig which had been passed by the bowels, are represented of the natural size. Fragments showing the structure are seen in figs. 105 and 106, pl. XII.

Vessels and nerves are to be demonstrated in some forms of adult yellow elastic tissue, but even in the ligamentum nuchæ they are very few in number. The yellow elastic tissue of the arterial coats seems to be nourished by imbibition only, and is completely destitute of nutrient vessels. The *nerves* for the most part belong to the capillary vessels, except in cases where muscular fibres are associated with the yellow elastic tissue, as

in the arteries, when numerous fine nerves are seen to ramify amongst the former fibres. This may be proved by examining the larger arteries of any small animal (frog, particularly the hyla, mouse, rat, rabbit.—L. S. B.)

Formation of Yellow Elastic Tissue.—With regard to the formation of yellow elastic tissue, different views are entertained. In his "Manual," published in 1860, and in former editions, Prof. Kölliker states, that these fibres are formed from cells, and he has given a drawing of "stellate formative cells of fine elastic fibres from the tendo Achillis (!) of a newly-born child." He says, that "in all parts of the embryo which afterwards contain elastic tissue, peculiar fusiform or stellate and sharply-pointed cells can be recognized, which, by their coalescence, produce long fibres or networks.* The fibres not unfrequently persist in this condition of stellate anastomosing cells, or connective tissue corpuscles (Virchow), as *e.g.*, in the tendons and the cornea, in ligaments and ligamentous discs, in the corium, in mucous membranes," &c. Kölliker agrees therefore with Virchow, in considering that these cells and fibres correspond to the canalicular systems of bones and teeth, and he proposes to call them *plasm*-cells, and their processes *plasm*-tubes, because they are supposed to convey *plasm* or nutrient juices.

In 1861, however, Prof. Kölliker completely abandoned his former views as to the fibres being formed from cells, and now maintains that the cells or nuclei which exist in such number at an early period of development have nothing whatever to do with the formation of the elastic fibres. He differs from Virchow as to the relation of the elastic fibres to the cells, and, so far from believing that they are continuous, maintains that the yellow elastic tissue represents *intercellular substance.* In the development of the ligamentum nuchæ, he says that the cells seen at an early period of development assist in the formation of an interstitial substance, "from which by independent *differentiation* both the connective tissue and the elastic fibrous networks proceed." By this term "differentiation," it is implied

* It may be remarked here that cells *never coalesce* during the development of tissue. Cells divide, and the subdivisions *separate* from each other—a fibre in many cases connecting them. This fibre of course increases in length as the cells become separated farther and farther from each other. Cells neither coalesce, nor do tubes or processes grow away from them and coalesce with tubes or processes from neighbouring cells, as has been asserted very positively by some authorities.

that from an interstitial substance originally homogeneous, connective tissue and yellow elastic tissue separate, or are deposited, or 'formify' (Owen), just as from a clear solution composed of two or more substances, may separate definite compounds exhibiting totally different forms and chemical properties. There is not, however, the slightest analogy between the two cases, and it is not remarkable that a view so strangely at variance with facts should have received little attention.

It has been already shown that the apparent fibres (Virchow's tubes) which resist the action of acetic acid and are embedded in the substance of the tendon, are not composed of elastic fibres at all, but merely consist of imperfectly formed tendon which, like other tissues at an early period of formation, resists the action of acetic acid. The formation of these apparent fibres is therefore to be accounted for without supposing, that like the gelatine-yielding fibrous tissue in which they lie, they result from the "differentiation" of an intercellular substance. It is not possible, nor would it be advantageous, to consider fully this long and very complicated question; but with regard to a form of true elastic tissue, one of us (L. S. B.) has remarked:—

1. That in the adult ligamentum nuchæ (sheep), masses of germinal matter (nuclei), are continuous with the material of which the yellow elastic tissue is composed, fig. 108, pl. XII.

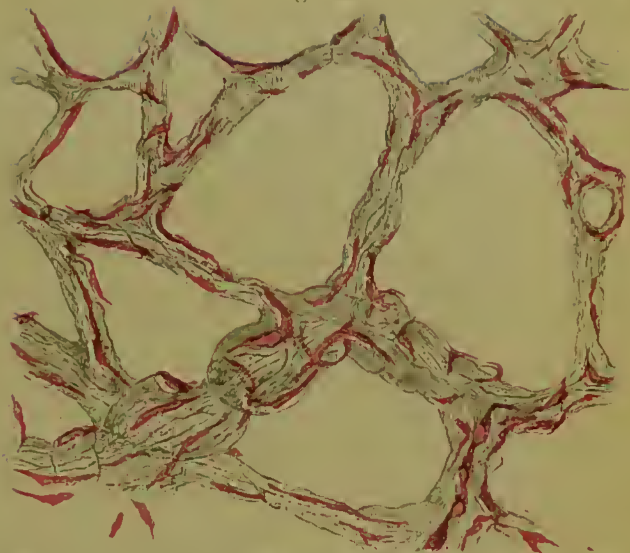
2. That these nuclei bear to the thick elastic fibres precisely the same relation which the "nuclei" bear to the white fibrous tissue of the adult tendon.

3. That in the ligamentum nuchæ of the lamb and young sheep, fibres of different ages and sizes may be obtained. The mode of development of the fibres may, in fact, be studied as well as in an embryonic tissue.

4. That in all cases the elastic substance results from the gradual conversion of germinal matter into this structure. In the ligamentum nuchæ and other parts where yellow elastic tissue is formed in quantity, the tissue may be traced into the masses of germinal matter. Elastic tissue never results from the differentiation of an intercellular substance. The germinal matter passes gradually into very soft, and this last into the fully-formed, tissue. The oldest portion of the tissue is that which is most distant from the germinal matter, as in other cases.

[illegible] of [illegible] elastic tissue. [illegible] mass of germinal matter [illegible] It has [illegible] is formed without the [illegible] germinal matter) [illegible] can be demonstrated [illegible] specimens. p. [illegible]

Fig. 104

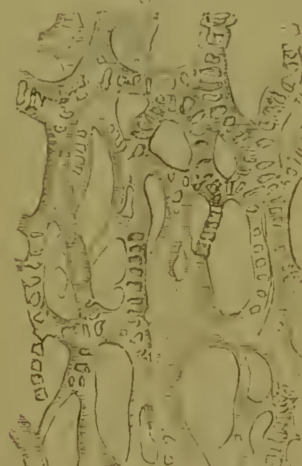


[illegible] of yellow elastic tissue encircling bundles of white fibrous tissue [illegible] beneath the mucous membrane of the ileum. Human subject, adult. × 215. p. 193.

Fig. [illegible]

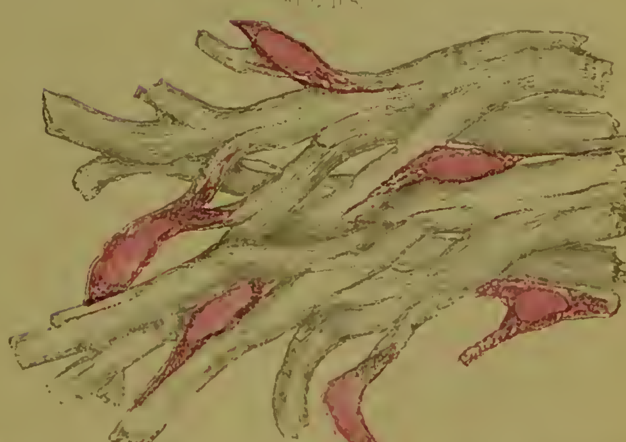
[illegible] a portion, probably of [illegible] S [illegible] nuclei of the glands. [illegible] p. [illegible] × 215. p. 100.

Fig. 106.



[illegible] elastic tissue. Showing the [illegible] markings. [illegible] by bowel. × [illegible] p. 200.

Fig. 108.



[To face p. [illegible]

5. What appears to be an ultimate fibre of such a tissue as the ligamentum nuchæ is not really so. It may be readily torn into very much finer fibres. In the case of young fibres, the nuclei are observed to be wider than the fibres themselves. After the elastic tissue has been formed, it gradually loses water and contracts, and the diameter of the fibre must necessarily be less than that of the nucleus up to a certain period of its growth. As the fibre grows in thickness, however, the "nucleus" is seen at its side just as in tendon. One of the thick fibres of the ligamentum nuchæ with "nucleus," therefore, corresponds to one of the small bundles of fibrillated tissue of tendon with its "nucleus." Compare figs. 103, 108, pl. XII., with fig. 100, pl. XI.

Fibres of Elastic Tissue which are not formed directly from Nuclei.—We have already seen that fibres closely resembling elastic tissue are embedded in a delicate transparent matrix with undoubted nerve fibres, and we have been able to trace fibres in various transitional conditions, from the nerve fibre to a structure resembling a fibre of yellow elastic tissue. There are, in mucous membranes, in the papillæ of touch and taste, outside the sarcolemma of muscle, and in other textures, fine fibres which form networks closely resembling the fibres of elastic tissue in general appearance, which are not formed from cells or nuclei, but which must be regarded as the remains of tissues, especially nerve fibres and vessels which were functionally active at an earlier period of life.*

In yellow fibrous tissue, from many situations, prolongations of germinal matter may be demonstrated as in other textures, but we have completely failed to prove the tubular character either of the fine or coarse yellow elastic fibres. Over and over again the nuclei amongst the fibres of yellow elastic tissue have been stained with carmine, as shown in figs. 103, 108, pl. XII, while not a single fibre exhibited the slightest alteration. Instead of the nuclei leading towards the central part of the fibre, they are invariably seen to be connected with the surface. Not a trace of germinal matter (nucleus) is to be found in the substance of any fibre of elastic tissue. It is therefore not probable that these fibres at any period of their development really consist of *tubes* for the transmission of nutrient juices.

* On the distribution of the nerve fibres to the mucous membrane of the epiglottis of man.—"Archives of Medicine," No. XII, page 250.

The portions of transparent material extending from the masses of germinal matter consist in fact of imperfectly formed tissue. Similar extensions from oval nuclei may be seen in some forms of voluntary and involuntary muscle. In some of the large elementary fasciculi of the voluntary muscles of the limbs of the old frog, they form quite a firm network, everywhere in the substance of the muscular tissue. This network has been regarded by some as constituting a system of nutrient tubes, by which the several nuclei are connected together as in tendon. By others the facts have been interpreted in a very different manner. These same lines have been regarded as *nerve fibres*, ramifying amongst the sarcous particles, with many of which they come into direct contact. Both views are, however, erroneous and untenable. The lines in question merely show that as the muscular fibre gradually increased in size, the masses of germinal matter which were originally continuous did not become completely detached from one another as the distance between them increased. We do not, however, consider that the facts allow us to regard them as of importance otherwise.

In *chemical constitution*, elastic tissue differs remarkably from the white fibrous tissue. It is unaffected by the weaker acids, or by boiling, and will resist putrefaction, and preserve its elasticity during a very long period. By very prolonged boiling, however, a minute quantity of a substance, soluble in water, which has been called teroxide of protein, and a trace of gelatine, derived from the areolar tissue and vessels, which always penetrate sparingly among its fibres, and cannot be separated by dissection, may be extracted from it.

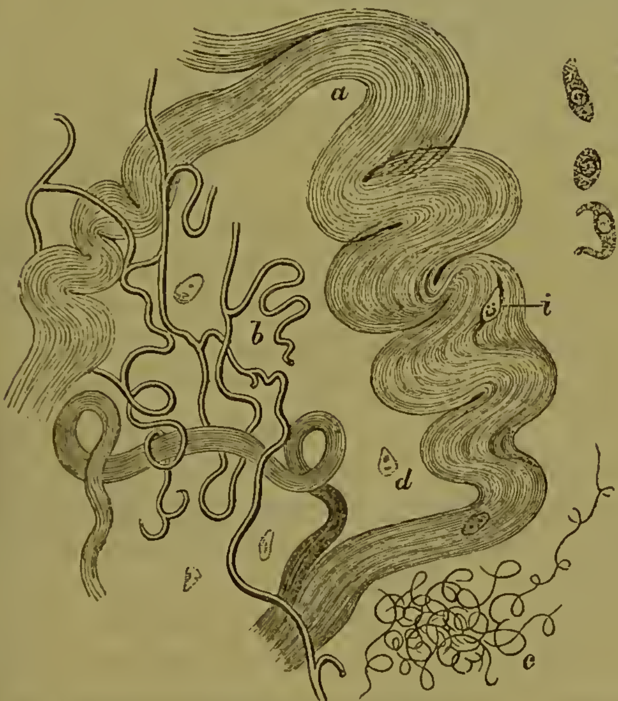
AREOLAR TISSUE.

In almost all parts of the body there exists a tissue consisting partly of the white and partly of yellow fibrous element. This texture allows great freedom of movement between different parts of an organ, and permits one texture to glide for a certain distance over another. It is a compound tissue, and has been called from its arrangement *areolar* (*areola* a small open place); but was formerly known as *cellular* or *filamentous tissue*.

Microscopic Characters.—When a fragment of well-developed areolar tissue is examined, it presents an inextricable interlacement of tortuous and wavy threads intersecting one another in

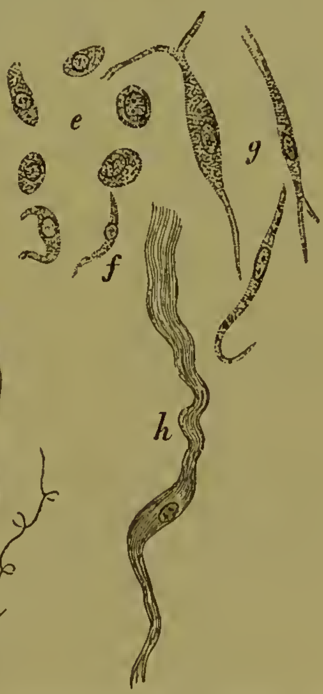
every possible direction. These are of two kinds. The first are chiefly in the form of bands of very unequal thickness, and inelastic. Numerous streaks are visible in them, not invariably parallel with the border, though taking a general longitudinal direction. These streaks, like the bands themselves, have a wavy character, but they are rendered straight by being stretched. The streaks seem to be marks depending upon longitudinal creasing, rather than the result of a true separation of the texture into actual threads. It is impossible by any art to tear up the band of fibrous tissue into filaments of a determinate size, although it manifests a decided tendency to tear lengthwise. The larger of these bands are often as wide as $\frac{1}{500}$ of an inch; they branch, or unite with others, here and

FIG. 115.



The two elements of Areolar tissue, in their natural relations to one another:—*a*. The white fibrous element, with cell-nuclei, *i*, sparingly visible on it. *b*. The yellow fibrous element, shewing the branching or anastomosing character of its fibrillæ. *c*. Fibrillæ of the yellow element, far finer than the rest, but having a similar curly character. *d*. Nucleolated cell-nuclei, often seen apparently loose.—From the areolar tissue under the pectoral muscle, magnified 320 diameters.

FIG. 116.



Development of the Areolar tissue (white fibrous element):—*e*. Nucleated cells, of a rounded form. *f. g. h.* The same, elongated in different degrees, and branching. At *h*, the elongated extremities have joined others, and are already assuming a distinctly fibrous character.—After Schwann.

there. The smaller ones are often too minute to be visible except with a good instrument. These are the *white fibrous element.* Fig. 115*a*.

The others are long, single, elastic, branched filaments, with a dark, decided border, and disposed to curl when not put on the stretch. These interlace with the others, and sometimes coil spirally round the bundles of white fibrous tissue, but appear to have no continuity of substance with them. They are for the most part about the $\frac{1}{8000}$ of an inch in diameter; but we often see, in the same specimen, others of much greater thickness. These form the *yellow fibrous element* (115*b*).

These two tissues, as already mentioned, may be most easily discriminated by the addition of a drop of dilute acetic acid, which renders the first clear and transparent without producing any alteration in the other. After the action of the acid upon the bands of white fibrous tissue, there often remains in them an appearance of more or less wavy transverse lines at pretty equal distances, remotely resembling those on the fibre of striped muscle. These are found to be very distinct, clear, and regular, and situated within short distances of one another in the fibrous tissue from the subcutaneous areolar tissue of the human embryo.

In the earliest period at which the areolar tissue can be examined, it consists of masses of germinal matter having offsets which are connected with one another. The formed material produced by these is at first homogeneous; the longitudinal streaks and the wavy character appear subsequently.

We have observed frequently among the threads of areolar tissue taken from adult subjects a number of corpuscles, fig. 115*d*, either isolated or having very delicate prolongations among the neighbouring threads. These seem with great probability to be either advancing or receding stages of the tissue (T. and B. 1843).

By the endless crossing and twining of the microscopic filaments, and of fasciculi of them, among one another, a web of amazing intricacy results, of which the interstices are most irregular in size and shape, and all necessarily communicate with one another. This is well seen by forcibly filling the tissue with air or water in any region. In the living body this is very obvious in œdema and anasarca, and in traumatic emphysema, as in the remarkable case related by Dr. W. Hunter in his celebrated paper (Med. Obs. and Inquir. vol. ii. p. 17), where the whole body was blown up so tensely as to resemble a drum.

The interstices are not, however, cavities possessed of definite limits, because they are open on all sides, and ultimately constituted out of a mass of tangled threads. The meshes which are formed are disposed so as to constitute secondary cavities,

Fig. 117.

Portion of Areolar tissue, inflated and dried, shewing the general character of its larger meshes. Each lamina and filament here represented contains numerous smaller ones matted together by the mode of preparation.—Magnified 20 diameters.

having a somewhat determinate shape and size, and which are visible to the naked eye. These sometimes contain fat, and may be admirably studied in most parts of the subcutaneous tissue. They communicate freely, as the smaller interstices do, their walls being everywhere cribriform, and capable of giving passage to air or fluids.

Some forms of connective tissue are represented in plate XIII. In fig. 119 is a drawing from a specimen of connective tissue covering one of the voluntary muscles of the hyla or green tree frog. The capillary vessels with their fine nerve fibres and the networks of fine nerve fibres distributed to the muscular fibres are well seen. The masses of germinal matter (nuclei) of the nerves are not connected in any way with those belonging to the connective tissue. The three figures 118, 119, and 120, in this plate should be attentively studied with the aid of the explanations beneath.

The areolar tissue is the most extensively diffused of all the tissues of the body, and its chief purpose seems to be that of connecting together other tissues in such a way as to permit a greater or less freedom of motion between them. To do this, it is

placed in their interstices, and is more or less lax, more or less abundant, according to the particular exigency of the part.

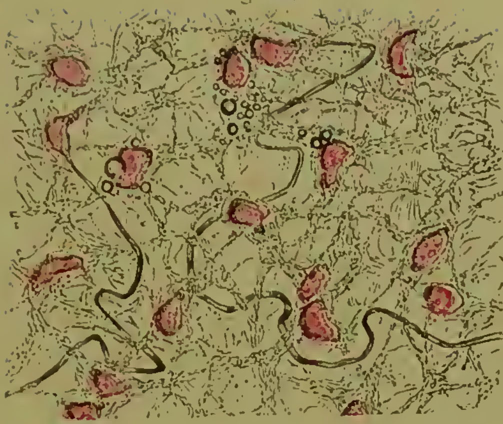
This form of areolar tissue, at least in all the larger animals, invests the exterior of the muscles in a profusion proportioned to the extent to which these organs move as a whole upon neighbouring parts, of which the best examples may be seen, between the great muscles of the extremities; between these and their enveloping fasciæ (not their fasciæ of origin); under the occipito-frontalis muscle and its tendon; and in the upper eyelids.

The areolar tissue is also present in immense quantities under the skin of most parts of the body, and especially where great mobility of the integument is required, either as a protection to deeper organs against external violence, or to facilitate the various movements of the frame. Such are the regions of the abdomen, and of several of the articulations, and the eyelids.

Around internal organs which change their form, size, or position in the routine of their functions, and which are wholly or partially without a free surface, as the pharynx, œsophagus, lumbar colon, bladder, &c., this tissue is abundant, and its filaments so long, tortuous, and laxly interwoven, as to admit of a ready and extensive motion on the neighbouring viscera.

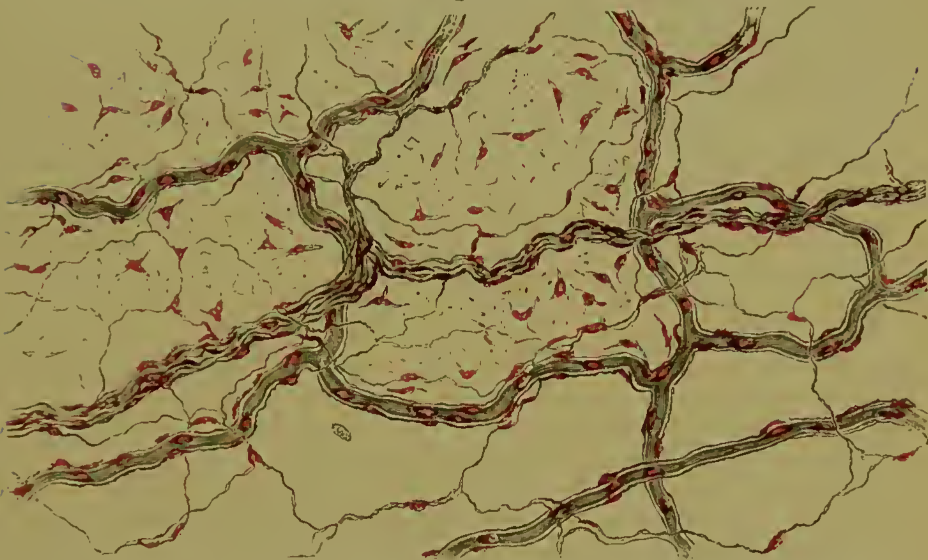
This tissue likewise forms a layer lying under the mucous and the serous membranes in almost every situation; though presenting great variations of quantity and denseness, it renders the movements of such parts easy. It also closely invests the exterior of every gland and parenchymatous organ, and enters more or less abundantly into its inner recesses, along with its vessels, nerves, and absorbents: but there is no doubt that it has been supposed to have a much greater share in the formation of this numerous class of organs than an ultimate anatomical analysis of them, conducted with careful precision, will at all warrant.—(T. & B. 1843.) In all these cases it is a more or less copious attendant on the vessels; but wherever, either from the intricacy of the interlacement of the capillaries with the other *essential* elements of the particular organ, or the greater strength of these elements themselves, the firm contexture of the whole is provided for, while little or no motion is required between its parts, this interstitial filamentary tissue will be found to be

Fig. 118.



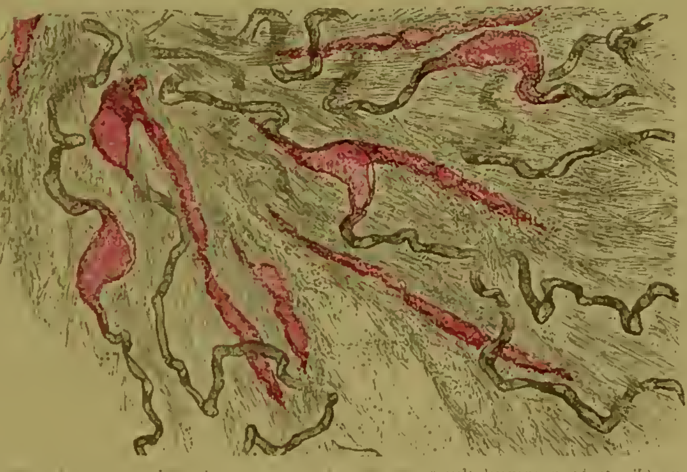
Simple fibrous connective tissue from the subperitonial connective tissue of a kitten two days old. Two fibres of yellow elastic tissue are seen. The proportion of germinal matter is very considerable. The manner in which the masses separate and form the intervening fibrous tissue is well shown × 215. p. 20[illegible].

Fig. 119.



Connective tissue covering part of the mylohyoid muscle of the hyla or green tree frog. *a.* Capillary vessels with their nerve-fibres. *b.* Bundles of fine dark-bordered nerve fibres, from which fine pale nerve fibres may be traced to the capillaries, and to their distribution in the connective tissue, where they form networks of exceedingly fine but nevertheless *compound* fibres. This drawing shows the arrangement of nerves in voluntary muscle; the muscular fibres having been removed, the course of the nerves can be readily traced. Magnified 700 diameters and reduced to 110. p 207.

Fig. 120.



Connective tissue from the submucous areolar tissue. Adult human subject. The masses of germinal matter taking part in the formation of the yellow elastic tissue, as well as those concerned in the production of the white fibrous element, are well seen. × 700. p. 207.

[To face p. 20[illegible].

confined to the larger blood-vessels, and to the *surface* of the natural subdivisions of the organ.

For the present, it may be sufficient to illustrate this remark by contrasting two important glands, in reference to this point. The human *liver* is well screened from injury by its position; it is liable to no change of bulk; it consists throughout of a continuous and close network of capillaries, the interstices of which are filled by the secreting cells. The lobules resulting from the distribution of the vessels and ducts blend together at numerous points, and have no motion on one another. Here the areolar tissue is in small quantity, and is almost limited to the larger ramifications of the vessels and ducts. The *mamma*, on the other hand, is, by its situation, peculiarly exposed to external injury. It is broken up into numerous subdivisions, which move with the utmost freedom on one another, and it is, moreover, liable to great temporary alterations of bulk. In this important gland not only is there a common investment of peculiar density, but an extraordinary abundance of areolar tissue disseminated throughout its interior.

Thus, this tissue, so widely spread throughout the body, whether it serve the purpose of an investment to large segments or masses, under the form of a membrane, strengthening and protecting them, and escorting their vessels and other components into and from their substance, or as a web of union between the simplest elements of their organization, is to be regarded as rather taking a subordinate or ministering share in the constitution of the frame, than as being of primary importance in itself. It is a connecting medium, that allows of separation between what it binds together; and it accomplishes this double purpose in a manner suited to the necessities of diverse parts, by a variety so simple in the number, intricacy, and closeness of its threads, as to be worthy of the highest admiration, while it is wholly inimitable by art.

The great value of areolar tissue in facilitating the motion of parts between which it is situate, is shown by the effects of inflammation or other diseases which injure its physical properties. It is well known that when the subcutaneous areolar tissue is the seat of phlegmonous inflammation, the movements of the part affected are stiff and painful, or altogether impeded, because the subjacent muscles cannot move freely by reason of

the loss of elasticity in the areolar tissue. When this tissue becomes indurated by an effusion of coagulable material, the movements of the parts adjacent are similarly impaired.

Where great elasticity is required, the yellow element preponderates; while the white fibrous element abounds in parts demanding tenacity and power of resistance. In all cases the openness of the network is proportioned to the extent of mobility required. Where the meshes are small, the threads composing them branch and anastomose with one another with much greater frequency. The texture of the cutis affords the most characteristic example of this condition.

Physical Properties.—These have only been studied hitherto in those situations where the tissue exists in great abundance, as in the subcutaneous fascia, the sheaths of muscles, &c. It has here a whitish hue, especially when steeped in water. It is extensible in all directions, and is very elastic, returning to its original disposition after stretching. In many situations it contains numerous fibres of unstriped or involuntary muscle, passing in different directions, which give to it the property of contractility, and in some of the lower animals voluntary muscular fibres are associated with it. These are very remarkably developed in the snout of the pig and in the nose of the mole, and are found in great number amongst the areolar tissue, beneath the loose parts of the skin of many other smaller animals (rat, mouse, mole). Nerve fibres are abundantly distributed in it, and its capillary vessels are more numerous than those of tendon.

This tissue, like many other soft solids, contains a large quantity of liquid, by which the filaments are kept moist and their physical properties maintained in a normal state. A morbid increase of this fluid in the subcutaneous areolar tissue occasions the condition called œdema and anasarca, which may be known by the skin *pitting.* Under the pressure of the finger, the fluid is driven into the surrounding areolæ or spaces, and a *pit* is made, but after the pressure is withdrawn the fluid returns slowly and the *pit*, or depression, disappears. When dried, areolar tissue becomes hard and transparent, but resumes its former state if placed in water. It undergoes the putrefactive process very slowly. It yields gelatin by boiling, but this substance is derived from the white fibrous element only.

Areolar tissue is in most cases associated with a certain proportion of adipose tissue, which will be described in chapter VII. In the following situations, however, we find areolar tissue without any traces of the adipose texture. Beneath the skin of the eyelids, in the median line of the abdomen, beneath the epicranial aponeurosis. The areolar tissue of the scrotum and penis is also destitute of adipose tissue.

It has been supposed that the nutrition of the areolar tissue, like that of the white fibrous tissue, is conducted through the intervention of tubes composed of yellow elastic tissue, but this question has been already referred to in page 203, and need not be further considered in this place.

Of the increase of Connective Tissue as Age advances.—The consideration of this subject of areolar or connective tissue has been much complicated by the circumstance that the areolar tissue just described, which is developed as a special structure for definite purposes, the fibrous connective referred to at the commencement of this chapter, and the connective tissue which is formed after the various organs and tissues are fully developed, have been included together under one head, as if they were all of the same nature, designed for similar purposes, and formed in the same way. It must be clear from what has been already stated that, although these textures resemble one another in some characters, they are not produced under the same circumstances, nor do they originate in the same manner. They also exhibit many remarkable differences in structure which require careful consideration.

Of these three forms, the last has not yet been considered at all; we therefore propose to refer to it in this place. Connective tissue appears to result in adult life from the decay of various textures, and the proportion increases as the individual advances in age. The change may be studied in many situations; for example, beneath the abundant plexus of dark-bordered and fine nerve fibres distributed to the mucous membrane covering the epiglottis, are numerous parallel fibres crossing and recrossing one another, which exhibit the reaction and general characters of yellow elastic tissue. These are found with numerous undoubted nerve fibres; amongst them are numerous delicate cords and bands of wavy tissue, like the cords of white fibrous tissue already referred to. Similar appear-

ances have been observed in certain of the papillæ of the human skin and tongue, and in other situations where plexuses of nerve fibres and vessels are abundant. In the beautiful papilla of the tongue of the hyla the structures in question are very distinct.* By alterations occurring in nerves and capillary vessels, fibres like the yellow elastic fibres of connective tissue result. The fact has been demonstrated in many different situations and in different animals, as man, the mouse, the cat, frog, and some others.

The actual alteration of nerve fibres into fibrous tissue has been very carefully studied in many localities. In the human organism the sole difficulty of following out the distribution of the nerves arises from the abundance of the connective tissue about them, and the difficulty increases as age advances.

Fibrous tissue also forms the residue of many other structures besides nerves and vessels; in fact, the variety which we are now considering is composed of the remains of various tissues which cannot be entirely removed by absorption. The connective tissue between the ultimate follicles of glands, that which surrounds vessels and nerves, and the fibrous tissue of which the so-called capsule of certain organs, liver, kidney, spleen, &c., are all in part or entirely of this nature. No wonder that in man, whose tissues pass through so many phases before they reach maturity, and in whom such active changes continually occur after this period, there should be a large amount of such a texture. This tissue, which is absent in the embryo at an early period, exists in very small quantity in the young child, but the proportion gradually increases as age advances. In small animals there is less than there is in large animals, and in young animals there is less than in old animals. In creatures of the simplest organization, whose tissues are, so to say, embryonic throughout the whole period of their existence, there is none. In all the higher animals whose textures uninterruptedly pass without cessation through many stages before they attain their perfect form, there is a large quantity.

This form of connective tissue also results in the course of certain degenerative processes occurring in higher tissues in disease. In various glandular organs which have undergone

* "New Observations upon the Minute Anatomy of the Papillæ of the Frog's Tongue."—Phil. Trans. June, 1864.

degeneration, a form of fibrous tissue remains behind. In cirrhosis of the liver, the fibrous matter which is present results not merely from the effusion and fibrillation of lymph, but is the remains of degenerated vessels, nerves, capillaries, ducts, and secreting tubes. In livers in this condition, properly prepared for investigation, vessels and shrunken secreting structure can always be demonstrated in the substance of the so-called "fibrous tissue" (L.S.B.).* The same remarks also apply to the kidney in certain cases of disease, and to other organs.

It is not to be wondered at, therefore, that this indefinite and unimportant connective material should have been made to play so very important a part in modern pathology. But if we are not mistaken, future observers will be much astonished at the rapid spread and general acceptance of the connective tissue doctrines. Connective tissue has been regarded as the actual seat of the active changes of inflammation and various forms of degeneration. It is supposed to become hypertrophied and then to contract, and by thus compressing glandular tissues to cause them to waste and bring about their destruction. We cannot, however, subscribe to these views, for careful observation compels us to conclude that in many forms of inflammation the connective tissue is passive, while the phenomena which have been wrongly attributed to it are mainly due to the presence of particles of germinal matter which have been detached from the white blood corpuscles, and have passed through the vascular walls into the meshes of the connective tissue, where they have grown and multiplied very quickly. These, and not the connective tissue corpuscles, are the bodies from which, in many instances, those collections of granular cells or corpuscles, pus corpuscles, and allied bodies, familiar to all who have studied the alterations occurring in tissues during the early stages of inflammation, originate. After the lapse of some little time, the germinal matter of the connective tissue corpuscles, as well as that of adjacent tissues, nerves, and vessels, participates in the changes, and in consequence of being freely supplied with nutrient matter, all these masses of germinal matter increase, divide and subdivide, and at length produce pus-corpuscles,† which do not result exclusively from the connective tissue

* "Archives of Medicine," vol. i, page 119.

† "On the Germinal Matter of the Blood," Microscopical Journal, 1863.

corpuscles or from white blood corpuscles only, but may be formed by any germinal matter which is very actively growing, and is the seat of increased nutrition.

Cord-like Fibres of Connective Tissue.—There are certain cord-like fibres in different localities in which we are able to study the mode of production of certain appearances which are observed in connection with some specimens of fibrous tissue of the higher animals, pl. XIV., fig. 121. The peculiarity referred to is this, that elongated fibres of a structure resembling elastic tissue seem to be embedded in a mass of white fibrous tissue. Many of these elastic fibres are connected together, and here and there nuclei are found. Often two branches seem to diverge from a nucleus, and the fibres vary much in diameter. Fig. 104, pl. XII; fig. 122, pl. XIV.

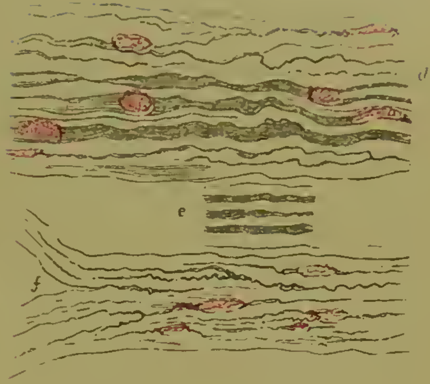
In several specimens of these cord-like fibres connected with the arteries, from the abdominal cavity of the frog, the following points may be observed:—A bundle of nerve fibres is perhaps seen running in the external coat of an artery. Some of the fibres leave the large trunk of the nerve and run in the central part of a fibrous cord, which is continuous with the areolar coat of the artery. A portion of one of these cords with most distinct nerve fibres may be seen in one part of a specimen, and in another, a transition may be traced from most undoubted nerve fibres to the very narrow branching elastic-like fibres just alluded to (figs. 121, 122, pl. XIV). These fibres are not altered by acetic acid, but by careful examination it is clearly proved that they may be split up into still finer fibres if they are not really composed of several delicate fibres collected together. They are not, therefore, merely fibres of yellow elastic tissue.

Some of the finest of these cord-like fibres of connective tissue consist of a transparent matrix in which two or three nerve fibres are embedded. The transparent tissue has been considered to be the so-called tubular membrane of the nerve fibre, but the term is inappropriate, inasmuch as the structure is of considerable depth and is not membranous. In some cases, several ganglion cells which were once connected with nerves, have wasted, and their remains, with those of the nerves proceeding from them, may be detected in one of these cord-like fibres of connective tissue. It seems to us, therefore, that

Fig. 121.

Connective tissue forming a network of rounded cords continuous with the areolar coat of a small artery. From the abdominal cavity of a frog. A part of the muscular coat of the artery is shown at *a*. A nerve is seen at *b* running in the external areolar coat. At *c* the bundle of nerve fibres are seen to divide × 130. p. 214.

Fig. 122.



Small piece of one of the cords represented in the upper part of Fig. 121 at *c*. Several nerve fibres are seen, and in the lower part of the drawing some very fine fibres, probably altered nerve fibres, are shown. At *e* another portion of a true but very fine nerve fibre is represented. From a portion of one of the finest cords in Fig. 121. Nuclei with branching fibres are seen at *d*, and the distribution of these is very similar to that of the fibres represented in the lower figure *f*. × 700. p. 214.

Fig. 123.

Development of young connective tissue, muscular fibres and nerve fibres, from beneath skin, back of very young newt. The large masses of germinal matter gradually undergoing conversion into three different kinds of formed material, connective tissue, nerve fibres, *b*, and muscular fibres, are well represented. In the centre of the drawing is seen a muscular fibre at the very earliest stage of its formation. *a*, a capillary vessel. × 7[illegible]0. p. 217.

[To face page 214.

the nuclei and delicate fibres continuous with them embedded in a more or less fibrous connective are, in many cases, the remains of nerve fibres which have been active at an earlier period of life, and that the matrix in which they are embedded and which corresponds to the so-called tubular membrane, results from the changes which have taken place in them as they have advanced in age.

In the dura mater, the coats of small veins undergo gradual thickening, until converted into solid bundles of fibrous tissue, and many have been seen with an exceedingly narrow cavity in the centre corresponding to the calibre of the vessel. This is another way in which solid cords of fibrous tissue may result.

There are other cord-like fibres in connection with some of the tissues of the frog, and which may also be detected in man and the higher animals, which are a little like those just described, but are formed in a very different manner. These are destitute of the peculiar fibres which resist the action of acetic acid above alluded to. Their mode of development may be clearly traced in the cutis of the frog. Numerous oval nuclei are seen undergoing division which occurs transversely and longitudinally, as in the formation of tendon already described. These are, in fact, bundles of tendinous fibres of the cutis.

It may be desirable that we should next offer a few observations upon certain fallacious appearances which may result from the method of preparing specimens of healthy tissues, and which have been a fertile source of erroneous generalization.

The smaller blood-vessels, both arteries and veins, when much stretched, appear as thin solid cords. In many specimens we have examined, had not the vessels been previously injected with transparent injection which could be traced up to one end of the apparent solid cord, and away from the other, the stretched transparent tube would certainly have been regarded as a solid cord of fibrous connective tissue. The nuclei which belonged to the vessel may be easily mistaken for connective tissue corpuscles. Capillary vessels, small ducts, the membranous tubes of certain gland textures from which the ephithelium has been removed, resemble very closely certain solid cords of connective tissue. The finer nerve fibres when stretched and pressed, have been mistaken for connective tissue, but when such fibres can be traced for a sufficient distance and proved to be continuous,

with dark-bordered nerve fibres, there can be no doubt concerning their real nature.*

With reference to connective tissue, it would seem, then, that there are:

1. Certain forms both of white and yellow fibrous tissue which are produced directly from germinal matter as other tissues, and in which masses of germinal matter may be demonstrated at every period of life.

2. Certain forms which may be regarded as the residue of higher tissues which have ceased to discharge active functions.

3. Certain forms of fibrous tissue (indefinite connective tissue), as in the papillæ of touch and taste, which result from changes having occurred in the terminal branches of the nerve fibres.

4. Certain forms of fibrous tissue, resulting from degeneration occurring in the course of disease (abnormal).

5. An appearance of fibrous tissue produced by pressure, crumpling, and stretching of nerves, capillaries, and other tissues.

In a compound structure like skin, a number of bodies, taking part in the formation of special tissues, have been dismissed under the term "connective tissue corpuscles." The following bodies, composed of germinal matter or bioplasm and generally termed nuclei, are certainly present:

1. Germinal matter (nuclei) of nerves. 2. Germinal matter (nuclei) of capillaries. 3. Germinal matter (nuclei) of white fibrous tissue. 4. Germinal matter (nuclei) of yellow fibrous

* Many writers in Germany who are displeased with my observations regarding the ultimate ramifications of the finest nerve fibres, because they happen to be incompatible with conclusions previously arrived at, and since repeated, that nerves terminate in ends or become continuous with other tissues, have not hesitated to affirm very confidently that my fine nerve fibres are merely "connective tissue," and this without ever having seen my preparations, or even examined my drawings with attention. They have, however, by this course placed themselves in a sad dilemma, for the fine fibres I have described can in every instance, and in many different tissues, be actually traced to distinct dark-bordered nerve fibres. My opponents must therefore maintain that the nerves terminate in fibres of connective tissue, or that dark-bordered nerve fibres (and if these, why not the whole nervous system?) are connective tissue. The latter view, however, it must be admitted is but a stage removed from the doctrine actually taught some years ago by some anatomists of the Dorpat School.—(L. S. B.)

tissue. 5. Germinal matter (nuclei) of fat cells. 6. Lymph, and white blood corpuscles.

In certain papillæ all the masses of germinal matter (nuclei) present, may be shown to belong to nerves and capillary vessels, and in the case of those between the elementary muscular fibres of the young mouse this is also strictly true. I do not think that in such situations, at least in young animals, there are any corpuscles which could properly be called connective-tissue corpuscles, nor have I succeeded in obtaining any facts which would favour the view that there are corpuscles of any kind distinct from the "cells" or "nuclei" (germinal matter) of the tissue, which perform special offices connected with the nutrition of higher tissues.—(L.S.B.)

At an early period of development many tissues, as yet imperfectly formed, may be mistaken for connective tissue. Thus nerve fibres, muscular fibres, and capillary vessels often escape identification in the embryo. And as the masses of germinal matter, or bioplasm, which take part in the development of these tissues cannot possibly be distinguished from one another, they are sometimes all regarded as connective tissue-corpuscles. See fig. 123, pl. XIV.

CHAPTER V.

OF CARTILAGE AND FIBRO-CARTILAGE.—PHYSICAL CHARACTERS OF CARTILAGE.—STRUCTURE.—PERICHONDRIUM.—VESSELS OF CARTILAGE.—OF FIBRO-CARTILAGE.—YELLOW ELASTIC OR SPONGY CARTILAGE.—FORMATION AND GROWTH OF CARTILAGE.—DEVELOPMENT.—CHANGES IN THE GERMINAL MATTER OF CARTILAGE.

Cartilage is extensively used in the animal frame, and is one of the simplest of the textures. In the development of the embryo, it is one of the first tissues to appear as a distinct structure, and it constitutes the internal skeleton in its earliest condition in the animal scale. The rudimentary skeleton of the cephalopoda consists of it; and in one class of fishes (hence termed cartilaginous, as the shark, ray, lamprey), the skeleton is entirely composed of cartilage.

In man and the higher animals, cartilage is employed, temporarily, as a nidus for bone, in the early stages of life, and is then called *temporary* cartilage. This, at a certain period, begins to ossify, and finally disappears by being converted into bone. At one time, the greatest part, not the whole, of the skeleton is cartilaginous; and for a considerable period after birth the extremities of the long bones are chiefly composed of cartilage, and the larger processes are connected to the shaft of the bone by this substance.

For other purposes, however, a cartilage is employed which is not prone to ossify, viz., *permanent* cartilage, and this is used either in joints (*articular* cartilage), or in the walls of cavities (*membraniform* cartilage).

The articular variety is either disposed as a thin layer between two articular surfaces, and equally adherent to both as in the synarthrodial joints (the cranial sutures, the sacro-iliac symphyses, &c.); or it forms an encrustation upon the articular ends of the bones entering into the composition of diarthrodial joints; thus, the extremities of the femur, tibia, the arm-bones, &c., are all coated with a layer of cartilage, moulded to the shape of the articular surfaces. The membraniform cartilages are not employed in connection with the locomotive mechanism, but serve to guard the orifices of canals or passages, or to form

tubes, that require to be kept permanently open; the elasticity of the material effecting this without the expenditure of any force. Thus we find this variety of cartilage in the external ear, in the Eustachian tube, in the nostrils and eyelids, and in the larynx, trachea, and bronchial ramifications.

Physical Characters.—Cartilage, in colour, varies from slightly bluish, or pearly white, to a whitish yellow. The temporary and articular varieties present the former colour; the membraniform, for the most part, the latter.

Elasticity, flexibility, and considerable cohesive power, are the chief physical properties of this texture; and in these qualities, and especially in the first, consists its great value, both in contributing to the perfection of the locomotive apparatus, and in its adaptation to other purposes. Cartilage is not very brittle. A thin piece, it is true, may be broken across by being suddenly bent at a very acute angle; but, in general, cartilage will bend easily without the occurrence of fracture, and will speedily resume its former direction on the bending force being removed.

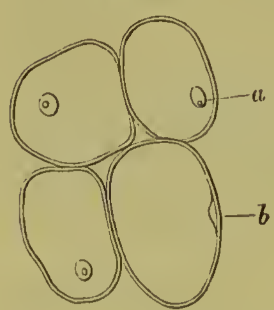
Structure.—The simplest kind of cartilage closely resembles some forms of the cellular tissue of plants. The cells or elementary parts may be very large, roundish or ovoidal, and more or less flattened by mutual contact. Each exhibits a mass of living growing germinal matter (bioplasm) containing within it one or more new centres (nuclei, nucleoli).

It is generally supposed that cartilage consists of *cells* and an *intercellular substance*, or matrix, and it is maintained by many that each cartilage cell possesses a very thin wall or capsule, distinct and separate from the cartilage matrix. By others, it is considered that the soft granular matter, just within the cell-wall, corresponds to the primordial utricle of plants—so that we may have,—passing from within, outwards: *a*, *nucleus*, *b*, *certain cell contents* (as not unfrequently *fatty matter*), *c*, *primordial utricle*, *d*, *external cell membrane;* and distinct from the latter, supposed to be deposited independently of it, the so-called *intercellular substance*, *e*. If these views are applied to the many different forms of cartilage, fibro-cartilage, and embryonic cartilage, the greatest difficulties will be experienced. Thus, the cell-wall cannot always be demonstrated as *distinct from the matrix*. Sometimes there is no proper *matrix* at all. In certain

forms fibres, resembling those of yellow elastic tissue, exist in the position of the intercellular substance, pl. XV, fig. 130, and in fibro-cartilage the *intercellular substance* resembles white fibrous tissue, pl. XV, fig. 133. The so-called primordial utricle or the "protoplasm" sometimes seems to be continuous in structure with the cell-wall, sometimes distinct from it. The "capsules" or "cell-walls" sometimes pass gradually into the intercellular substance, and as these are formed one within the other from the "cells,"* the latter must, therefore, at least *take part in the formation of the intercellular substance;* but it is maintained that intercellular substance is formed without the agency of the cells.

We might adduce very many conflicting statements with regard to the anatomy of the simplest form of cartilaginous tissue, but we shall follow the same plan adopted elsewhere, and describe the appearance we have ourselves been able to observe. The simplest cartilage is found in the chorda dorsalis, or rudimentary spinal column of the early embryo: it also exists in the permanent chorda dorsalis of the cartilaginous fishes, and may be well seen in a thin piece of that structure from the lamprey, fig. 124.

Fig. 124.



Four nucleated cells from the Chorda Dorsalis of the Lamprey:—*a.* Nucleus, with nucleolus. *b.* Another, seen in profile.

But, in other kinds of cartilage the germinal matter is imbedded in formed material which may form—1, a capsule surrounding the germinal matter (cell-wall), or 2, a continuous mass called *intercellular* substance, or matrix, more or less abundant in the different kinds, and presenting certain varieties of appearance. A "cell" of cartilage, therefore, consists of the germinal matter with a proportion of formed material around it, whether this appears separate and distinct, forming a capsule, or continuous as matrix or intercellular substance. See pls. XV, XVI, page 230.

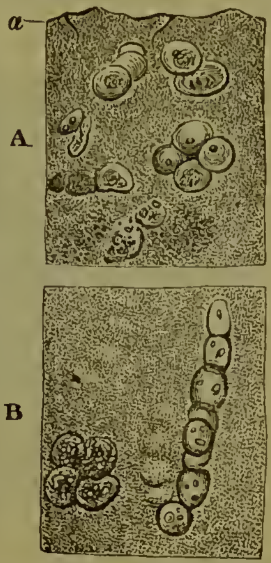
In *temporary* cartilage the masses of germinal matter are very numerous, and situated at nearly equal distances apart in the intercellular substance, which is not abundant. They vary in shape and size, but most are round or oval. When ossification begins, the cells, which hitherto were scattered without definite

* See a paper on "Connective Tissue," by Dr. Martyn, in my "Archives," vol. ii, p. 110.

arrangement, become disposed in clusters, or rows, the ends of which are directed towards the ossifying part. These and other changes will be described in the next chapter.

In *articular* cartilage the cells are oval or roundish, often disposed in small sets of 2, 3, or 4, irregularly disseminated through a nearly homogeneous matrix, which is more abundant than in the last-named variety; fig. 125, A. The cells measure from $\frac{1}{1300}$ to $\frac{1}{900}$ of an inch. The "nuclei" are for the most part small. In the interior part of the cartilages of encrustation we usually find the cells assuming more or less of a linear direction, and pointing towards the surface; fig. 125, B. This arrangement is probably connected with a corresponding peculiarity of texture of the intercellular substance, but which it is more difficult to distinguish; for these specimens have a disposition to fracture in a regular manner along planes vertical to the surface, and the broken surface is striated in the same direction.

Fig. 125.



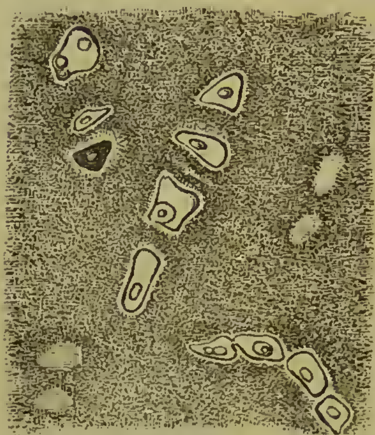
Articular cartilage, from the head of the Humerus:—Vertical sections: A. Section close to the surface, *a*. B. Section far in the interior.—Magnified 320 diameters.

Near its deep or attached surface, articular cartilage blends gradually with the bone it invests. The cells in the neighbourhood are surrounded with a sprinkling of fine opaque granules, which seem to be a rudimentary deposit of bone. The true bone dips unevenly into the substance of the cartilage.

A pavement of nucleated epithelial particles has been described by Henle to exist on the free surface of articular cartilage. In the foetus this may be readily seen; but in the adult we have failed to detect it, even in perfectly fresh specimens, and notwithstanding great care. The articular cartilage of the adult is naked in the cavity of the joint, and very gradually wears away by friction as age advances. An irregularity of surface, like that represented in fig. 125, *a*, often exists, and seems to show that the epithelial covering ceases when the part becomes subject to friction and pressure. Cells, too, are often seen close to this surface, and even partly projecting from it; appearances clearly indicative of attrition.

In the *cartilages of the ribs*, which occupy an intermediate place between the articular and membraniform varieties, the masses of germinal matter are larger than in any other cartilage in the body, being from $\frac{1}{650}$ to $\frac{1}{130}$ of an inch in diameter. Many of them contain two or more particles of bioplasm "nuclei," which are clear and transparent; and some contain a few oil-globules, a condition occasionally met with in other varieties. They often affect a linear arrangement. The rows of the masses of germinal matter are turned in all directions, and have the appearance of having been formed by the division of one, and the separation of its parts from each other in a continuous line.

Fig. 126.



Cartilage of the Ribs. Section showing the germinal matter (nuclei and nucleoli). The transparent spaces result from the removal of the cells by the knife, their cavities remaining.—Magnified 320 diameters.

The formed material "intercellular substance" is very abundant in these cartilages; and though it usually presents, on a section, a very finely mottled aspect, such as is very correctly pourtrayed, in the figure, yet we may often discern it in an appearance like fibrous structure, in which the apparent fibres are in many cases parallel. This is most evident in the aged. It is probable that the appearance in question depends upon a tendency to cleave or split on the part of the tissue. The lines in question have very little resemblance to those seen in white fibrous tissue.

In the true *membraniform* cartilages, the masses of germinal matter are very numerous in proportion to the surrounding substance, which is consequently in small quantity. This matrix is very distinctly fibrous towards the exterior of these cartilages, where it passes into the perichondrium. The thyroid and cricoid cartilages, and the rings of the trachea, seem chiefly, composed of clearly defined and roundish nucleated cells huddled together, as it were, in a promiscuous

Fig. 127.

Thyroid Cartilage:—Thin section.—Magnified 320 diameters.

manner, fig. 127. In the cartilages of old persons, the matrix near the masses of germinal matter not unfrequently becomes infiltrated with calcareous matter and thus a form of osseous tissue results.

In the *cartilage of the ear* the cells are small, and very close to each other; in shape they are very uniform, and vary in size from $\frac{1}{1300}$ to $\frac{1}{700}$ of an inch. The formed material "intercellular substance" is not exactly white fibrous tissue; but so nearly resembles it, especially towards the surface, as to make this form of cartilage approach fibro-cartilage more nearly than does any other.

Cartilage of the Ear of the Mouse.—A very interesting form of cartilage which seems to consist entirely of separate cells packed closely together, as in ordinary epithelium, is to be obtained from the delicate membraniform cartilage of the ear of the mouse and other small animals. At short distances from one another, are holes, which in the dissected or partially macerated cartilage, are seen to pass right through, giving it a cribriform appearance if examined by low powers. In a carefully prepared and injected specimen, it will however, be found that these spaces are occupied by vessels and nerves, which pass through them from one perichondrial surface to the other. The cells at the margins of these openings are very small, and in fact the new cartilage is formed in these situations. By making very thin sections through the tissue, "cells" of every age may be discovered, and the mode of division of the germinal matter, and the production of the formed material corresponds in all essential particulars with what takes place in other forms of cartilage. It is remarkable that the production of fat should be associated with the formation of cartilaginous texture in this form of the tissue. Each of the so called "cells" might almost be described as a fat vesicle, the walls of which are composed of cartilage instead of delicate transparent membrane, but this will be considered in connection with adispose tissue in chapter VII. *See* fig. 132, pl. XV., page 230.

Perichondrium.—The membraniform cartilages are invested by a layer of white fibrous tissue, containing blood-vessels, and called the *perichondrium.* Its fibres are densely interwoven in all directions, and adhere intimately to the intercellular substance of the cartilage. This investment corresponds with

the periosteum of bone, and in the temporary cartilages is indeed the very same structure. In connection with the perichondrium ramify the nutrient vessels of cartilage, and it serves to give attachment to muscles. It is in fact continuous on the one hand with the formed material or matrix of the cartilage, and on the other with that of the tendon. This fact is well seen in the thin section through tendon periosteum, and cartilage represented in fig. 129, pl. XV. It is best examined on the cartilages of the ribs. Its great toughness is sometimes well displayed in fractures of these cartilages, where the perichondrium remains untorn between the fragments.

The articular cartilages, which have no perichondrium, are supported and supplied with blood by the bone to which they are adapted, and by the synovial membrane, which extends for some little distance over their free surface.

Vessels of Cartilage.—Speaking in general terms, cartilage may be styled a non-vascular tissue, for considerable masses of all its varieties exist, unpenetrated by a single vessel. The term *non-vascular*, however, it is important to observe, is to be understood in a relative sense. All tissues deriving their nutriment from the blood circulating in the vessels, are, in fact, if traced up to their microscopic elements, on the outside of the channels through which the blood flows. If the quantity of vessels be large in proportion to the tissue, or if the two are mingled in an intimate manner, we term the part very vascular. If, on the other hand, there be a considerable mass of tissue, among the elementary parts of which no vessels penetrate, it is styled non-vascular. This word is not used in an absolute sense; for, if so used, it would apply equally to all tissues, except the lining membrane of the vascular system itself, which is nourished by the blood immediately in contact with it.

Returning from this digression, we remark, that temporary cartilage, when in small mass, is not penetrated by vessels; but that, when more than about an eighth of an inch thick, it contains canals in its substance, for the transmission of vessels. These canals are somewhat tortuous, and contain a delicate extension of the perichondrium. They may be regarded as so many involutions of the outer surface of the cartilage. The same description will apply to the various membraniform car-

tilages, with this difference, that their blood-vessels are less numerous. In those which are thin, no vascular canals are to be found; but where there is much substance, as in the costal cartilages, they are easily detected.

Nothing is more certain than that articular cartilage, in man, is not penetrated by blood-vessels. Coloured fluids injected into the vessels cannot be made to enter it, but are seen to turn back, on reaching it, into the tissue which conveyed them to it. But we possess a more certain test than this, in the examination of thin slices of the tissue under a high power. This brings no vessels into view; on the contrary, it proves their non-existence beyond dispute. In some diseased states, however, a few vessels may be demonstrated. Mr. Toynbee (Phil. Trans., 1841,) has pointed out, that the vessels of bone, at the part on which cartilage rests, are separated from the cartilage by a bony lamella, in which no apertures exist. The minute details, on approaching this lamella, dilate, and form loops with the convexity towards the cartilage. The vessels after forming arches, run back into the cancelli of the bone. Such an arrangement must, of course, be attended with a retardation of the blood near the "articular lamella." The vessels of the synovial membrane advance with it a little way upon the articular surface of the cartilage, but only over those parts which are not subject to pressure during the natural movements of the joint. These likewise terminate in loops. In diseased states they often advance much further upon the cartilage than they do naturally.

Of Fibro-Cartilage.—This texture is a compound of white fibrous tissue and cartilage in varying proportions. It is principally employed in the construction of joints, and contributes to their perfection at once by its strength and its elasticity; but as it is also, to a limited extent, used for other purposes, it may be conveniently described as 1, Articular; 2, Non-articular.

Fibro-cartilage, examined by the naked eye, has much of the colour and general appearance of the thyroid cartilage, or of other examples of the membraniform variety, which Bichat, indeed, clased among fibro-cartilages. Its colour is white, with a slight tinge of yellow; it is interspersed by the shining fibres of white fibrous tissue, and its appearance differs with the quantity of that texture that is mingled with it. Its consistence

also varies, for the same reason; in some instances being extremely dense, in others soft, yielding, and almost pulpy. When examined microscopically, fibro-cartilage is found to consist of bundles of wavy fibres, with the cells or corpuscles of cartilage occupying the spaces formed by the interlacement of the fibrous tissue. This interlacement is often very intricate, and calculated to increase the strength of the structure in those directions in which the greatest toughness is required.

Physical Properties.—To the strength and density of fibrous tissue, fibro-cartilage adds the elasticity of cartilage; it is more variously flexible than the latter tissue, so that it will not crack when bent too much. Fibro-cartilage contains water; when deprived of it by drying, it shrivels up, and becomes hard and yellow. It yields gelatine in abundance on boiling.

Vessels and Nerves.—Its vessels are few, and are derived from the textures (synovial membrane or periosteum) with which it is in immediate connexion. Few nerve-fibres are to be demonstrated in this tissue.

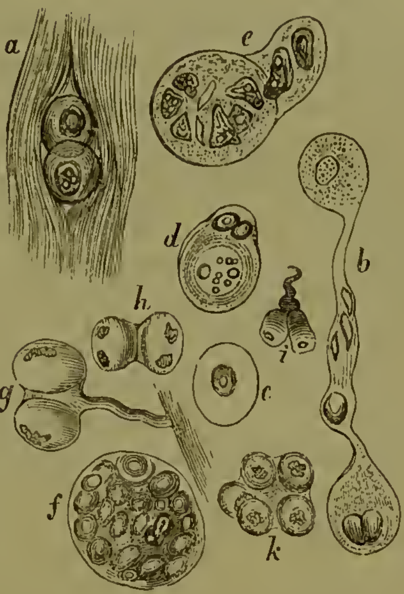
Forms of Fibro-cartilage.—The *articular* fibro-cartilage is that which is found most extensively, and it exists in three forms. *a.* As *discs*, interposed between osseous surfaces, and equally, adherent to both, of which the intervertebral discs and the interpubic fibro-cartilage are instances. *b.* As laminæ, free on both surfaces, placed in the cavity of diarthrodial joints between the articular surfaces of the bones. These are the *menisci* of authors; they exist in the temporo-maxillary, the sterno-clavicular, and the knee joints, and between the scaphoid and lunar and cuneiform bones. *c.* As triangular edges to the glenoid and cotyloid cavities of the shoulder and hip joints. These are styled *circumferential.*

In examining these different forms of fibro-cartilage, some varieties are met with deserving of a brief notice.

The *intervertebral discs* consists of concentric layers of white fibrous tissue, placed vertically between the surfaces of the vertebræ: although the layers are vertical, the fibres of which each layer is composed, are directed obliquely from above downwards, and the direction of the fibres of one layer is such as to decussate with those of the layer immediately behind it. Each pair of layers of fibrous tissue is separated by a lamina of cartilage. This arrangement belongs to rather more than the

outer third of the disc: the central portion is occupied by a soft, yielding, pulpy matter, which, when a disc is cut horizontally, rises up considerably above the surrounding level. This soft mass consists of a few bundles of white fibrous tissue (wavy fibres), with numerous cell-like bodies very variable in shape and size, loosely interspersed. It is girt by the surrounding vertical fibrous layers and their interposed cartilaginous lamellæ, and also compressed by the vertebræ between which it is placed; the pulpy matter being separated from immediate contact with the surfaces of the vertebræ by the interposition of thin layers of cartilage.

Fig. 128.



Elementary structures from an intervertebral disc; *a.*—Two cartilage-cells lying amongst the white fibrous tissue. The remaining objects are from the central pulpy substance, and exhibit various forms of cell. In several of these there is an appearance of multiplication by subdivision of the nucleus, and some seem attached by a fibrous tissue. The full meaning of this does not yet appear.

In the *menisci*, the white fibrous tissue predominates considerably at their circumferences, while the cartilage chiefly abounds in the centre. Those of the knee joint and temporo-maxillary joint are the densest; that of the sterno-clavicular is softer and more cartilaginous.

The *circumferential* fibro-cartilages contain a considerable predominance of fibrous tissue.

The *non-articular* form of fibro-cartilage is found lining the grooves in bones, which lodge tendons; as, for example, the groove for the lodgement of the tibialis posticus. In intimate structure it resembles the articular forms.

Reparation and Reproduction.—Fibro-cartilage heals by a new substance of similar texture. Sometimes the union of bone is effected by a material of this kind, in cases where osseous union cannot be obtained.

Yellow Elastic or Spongy Cartilage.—The distinctive character of this form of cartilage is, that the formed material consists in great part of fibres somewhat resembling those of yellow elastic tissue, and like these, resisting the action of acetic acid.

The student may obtain interesting specimens of spongy elastic cartilage from the cartilage of the lobe of the ear, from the epiglottis of the human subject, or from the arytenoid cartilages of man, the ox, or sheep. It has been supposed that the fibres of this form of cartilage, which resist the action of acetic acid, and agree in general characters with elastic tissue, result from changes which have spontaneously occurred in the so-called *intercellular-substance.* Some have considered it a sufficient explanation of the process to attribute it to "fibrillation" or to "differentiation" of the matrix, and seem to think that the elastic fibres simply crystallise out, as it were, forgetting, however, that the elastic tissue cannot be detected in the fluid corresponding to mother liquor from which the crystallisable matter separates. If a thin section of the epiglottis be attentively examined with a high power, the angles of the masses of germinal matter may be seen to be continuous with the fibres. In short, there is little doubt that as the germinal matter moves about in these spaces, the fibres are slowly formed one within the other until that highly complex concentrically arranged network of fibres characteristic of the fully formed tissue results, see fig. 130, pl. XV, which represents the appearance seen in a very thin section cut parallel to the flat surface near the circumference of the epiglottis.

Formation and growth of Cartilage.—All observers are agreed that at an early period of development every form of cartilage consists almost entirely of bodies termed cells. But at this time these "cells" have no cell-wall, and the material of which they consist is continuous with the small amount of transparent matter in which they lie, and which forms a very thin layer, separating them from one another, fig. 134, pl. XVI. We may therefore say, that at first cartilage consists of roundish masses of germinal matter or bioplasm, embedded in a small quantity of soft transparent formed material. It is only necessary to investigate carefully the alterations which occur during development in this simple typical structure. As in other cases, in the perfectly fresh tissue the germinal matter is continuous with the formed material. Sometimes, after death there is an appearance as of masses with a well-defined outline distinct from the formed material, and hence has arisen the notion of cells with distinct cell-walls. But any mass of germinal matter placed in water

will exhibit a sharp outline. This has been considered to indicate the existence of a "cell-wall."

The masses of germinal matter at first are very close together; they divide and subdivide as they lie in the soft formed material, and, as development proceeds, become separated from each other by gradually increasing intervals. At the same time, the formed material undergoes slow condensation, and the formation of new formed material on the surface of each mass of germinal matter more than compensates for the shrinking of the already-formed matrix, which takes place. Each of these masses of germinal matter divides and subdivides, and formed material is produced on the outer surface of each, so that there are small collections of masses of germinal matter separated from each other by a considerable extent of formed material in the shape of fully-formed cartilage, while the separate masses composing each collection are themselves separated from each other by a very thin layer of recently produced and much softer formed material, fig. 131, pl. XV *a*, *b*, *c*, *d*. Thus the gradual condensation of the first produced formed material proceeds without shrinking of the entire mass, and without the formation of large cavities. The division and subdivision of the original masses of germinal matter proceed, and the formation of new formed material advances, but more and more slowly, as the condensation of that already produced goes on. For some time the entire mass of cartilage continues to increase in bulk, and at the same time becomes less permeable to nutrient fluids.

The masses of germinal matter of cartilage differ in form in different varieties of cartilage, and in the same kind at different ages. As in all other tissues, at the earliest period of development they are spherical, and in some instances this form is retained throughout life, but more commonly they become oval or of an irregular ovate shape. Not a few, especially in growing cartilage, when division is proceeding, are like a hemisphere, fig. 141, *b*, pl. XVI. Sometimes they are angular, fig. 140, pl. XVI, or of very irregular form. At certain periods of growth, some appear as rings, as represented in figs. 137, 138, pl. XVI, or of semilunar form.

The mode of production of these last forms will be understood by reference to figs. 135, 137, 141, pl. XVI. But the most remarkable shape which the masses of germinal matter of car-

tilage assumes is stellate, the processes of one mass being continuous with those of others, resembling very closely the arrangement of the so-called stellate cells of the cornea, and certain connective tissue corpuscles, fig. 94, pl. X, p. 182.

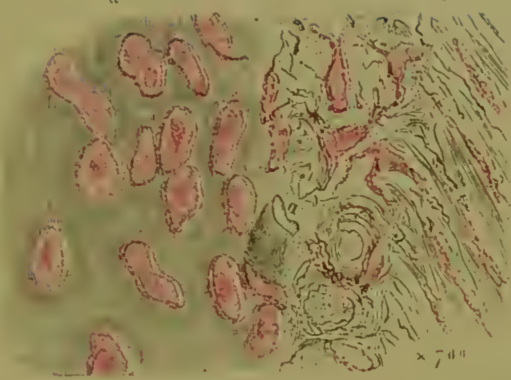
The germinal matter of cartilage exhibits the same general characters as that of other tissues. In some cases, one new centre (nucleus) only is seen in each; in others, two or more. In inflamed cartilage, each mass of germinal matter may contain several new centres (nuclei, nucleoli), and these may increase in size, and give rise to new series within them.

Movements in the living germinal matter have been seen by Heidenhain, who induced them by causing an electric current to traverse the cartilage. The form of the masses was much altered, but at length coagulation, consequent upon the death of the living matter, took place. Movements occur in every form of germinal matter, but they can only be observed in some tissues. Cartilage and the cornea are among the most favourable for observation.

Development.—The mode of development of cartilage will be understood by reference to the drawings in pl. XVI. In fig. 134 large oval masses of germinal matter are seen to be separated from each other by a very thin layer of soft formed material (matrix), which is slightly granular, but it is not coloured by the carmine solution. In fig. 135 the mass of germinal matter has increased in size, but as this substance grows, the conversion of its outer portion into formed material proceeds, and therefore the entire elementary part, consisting of germinal matter and surrounding formed material (cell and corresponding portion of matrix) becomes larger. The next stage is shewn in fig. 136. Several zones, exhibiting different shades of colour, are now seen; the outer one, which passes into the formed material, being the most faintly, the innermost portion of the germinal matter (nucleus), the most darkly, tinted, although to reach this the solution must have passed through all the outer layers. In figs. 137, 138, *growth* of the entire elementary part seems to have ceased, but the conversion of the oldest part of the germinal matter into formed material proceeds, until at last only a small portion remains, and this in many instances dies and an oval collection of granules, which are not tinged red with carmine, fig. 139, is all that marks the position of the

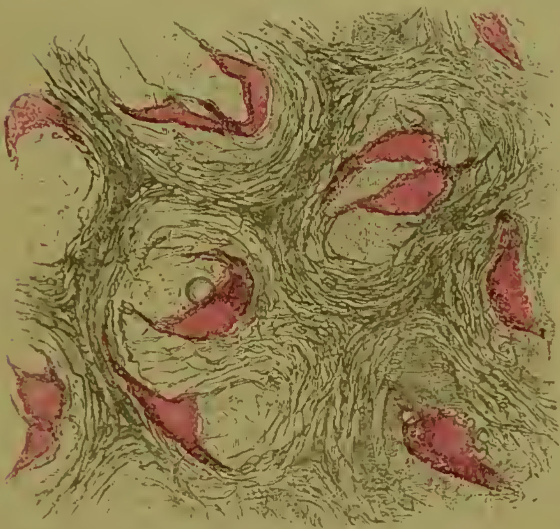
PLATE XV.

Fig. 129.



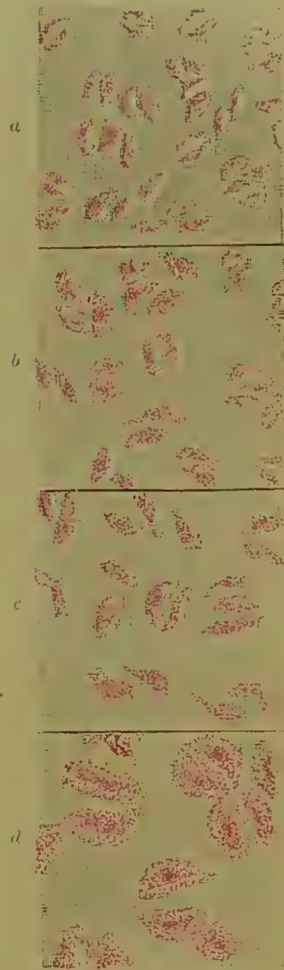
Junction of cartilage with tendon. Os calcis of a kitten very soon after birth. *a* is the temporary cartilage which will be converted into bone. *b*, corresponds to the periosteum of the future bone, and *c* is the tendon. *a*, near the centre of the figure, is a capillary. × 700. pp. 190, 224, 233.

Fig. 130.



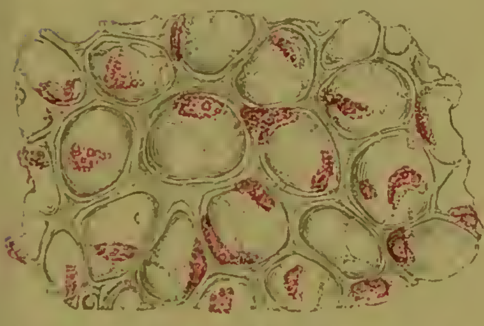
[illegible] elastic or spongy cartilage. Epiglottis, human subject. [illegible] masses of germinal matter in the spaces and the manner [illegible] they form the elastic fibres are given. × 700. pp. 16[illegible] 2[illegible]

Fig. 131.



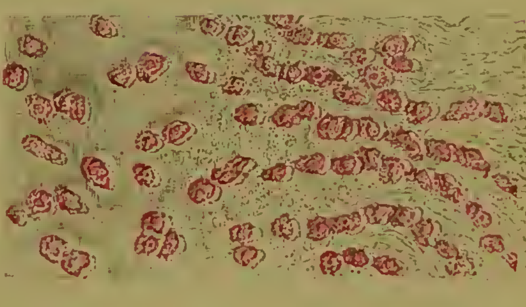
Cartilage at different ages. *a*, kitten at birth; *b*, six weeks old; *c*, nearly full grown; *d*, adult cat. × 215. Showing alteration in the relative proportions of germinal matter and formed material at different ages. p. [illegible]9.

Fig. 132.



[illegible]rtilage from the thinnest part of the [illegible] of the white mouse. The spherical masses of highly refracting matter are oil-globules. The oval masses of bioplasm [illegible] form these and the cartilaginous tissue are [illegible] × 2[illegible] [illegible]3[illegible]

Fig. 133.



Fibro-cartilage. From the intervertebral disks. [illegible] at birth. To the left the matrix presents the ordinary character of cartilage, while on the right it has a fibrous appearance. × 215. pp. 228, 233.

[To face page 2[illegible]]

mass of germinal matter by which the surrounding matrix, or formed material, has alone been produced. After this has occurred the matrix may become harder and undergo other changes, but no more can be formed. The *formation* of the matrix in this particular spot has ceased. The matrix, which is recently formed and which shades into the germinal matter is of course soft, and when it is broken through, the mass of germinal matter within may escape entire. In all tissues the bond of union between the germinal matter and formed material is very slight; a fact which receives a simple explanation upon the view of growth brought forward. The mass of germinal matter which has been thus removed becomes smooth upon its outer part and its well-defined outline has been considered to be due to a cell wall, which has been described as distinct from the wall of the cavity in which the "cell" is supposed to lie.

In the formation of cartilage, it has been said that the supposed membranous capsule of the cartilage cell *sends in septa* when the matter it contains undergoes division "which serve as new envelopes for the young cells, yet in such a way, that even the gigantic groups of cells, which proceed from each of the original cells, are still enclosed in the greatly enlarged parent capsules." (Virchow). Against this theory, one of us L. S. B. has endeavoured to show that the matrix or intercellular substance with the membranous capsules of the cartilage cells is passive and possesses no such capacity of *sending in* septa. Like the cell-wall of a spore of mildew to which it corresponds, it does not possess formative power. It *has been* produced. It has been formed, but it cannot *form*. It may be added to, but it cannot increase or build itself up out of pabulum. The outer capsule of the mildew, never possesses inherent powers of growth. It is the internal germinal matter or bioplasm which is alone concerned in the growth of the plant. So in cartilage, the matrix is passive. The germinal matter only possesses active power. The septa do not *extend themselves in*, *or grow in*, but the material of which they are composed results from an alteration taking place upon the surface, that is in the oldest part of the germinal matter, fig. 141, at *a*, and *c*, pl. XVI.

It is certain, that the matrix is never produced without the masses of germinal matter, nor can it increase except by their agency. In disease change is observed in the rate of growth of

the bioplasts. After the matrix has been produced many of the masses of germinal matter may die and disappear, but in growing cartilage they are invariably present. The living matter, of which the germinal matter consists, is always continuous with the more or less transparent matrix. The living matter gradually becomes converted into the matrix. There is no appearance of a cell-wall distinct from the matrix, as some maintain, nor is there an interval between the living matter and the matrix, unless post-mortem change has occurred. The first passes uninterruptedly into the last, pl. XVI, fig. 140. The ragged outline of many of the masses of germinal matter in the cartilage from the frog renders the terms "cell nucleus," "cell contents," or "granular corpuscle," totally inapplicable, and it is clear that around such masses there can be no cell-wall. The germinal matter gradually *becomes* the matrix, and all matrix was once in the state of germinal matter, as all the matter in the living or germinal state was once in the condition of pabulum. Without germinal matter there *can* be no cell-wall or intercellular substance. In all cases pabulum is converted into germinal matter by pre-existing germinal matter, and this last is at length converted into formed material, be it fluid or solid, cell-wall, secondary deposits, or intercellular substance.

We shall find when we come to consider the anatomy of bone, that the first deposition of calcareous particles takes place in the formed material at a point midway between the masses of germinal matter—that is, in *the oldest portion* of the formed material, fig. 144, pl. XVII. The deposition of the calcareous matter can be explained by physics, and can be imitated out of the body, but the matrix which is formed cannot be produced artificially. This results from changes occurring while the matter of which it consists was in the state of living germinal matter.

The fibrous tissue of tendon is continuous with the matrix of the cartilage, and the gradual transition from the clear transparent cartilage matrix to the fibrous tissue of the tendon may be well traced in fig. 129, pl. XV, p. 230. So, the contractile material of muscle is continuous with the fibrous tissue of tendon, and the masses of germinal matter (nuclei) in the two tissues exactly correspond. The formed material in each tissue is continuous, and the masses of germinal matter

bear to it a similar relation. The *formation* of cartilage, tendon, or muscle depends—1, upon the vital powers of the germinal matter which becomes converted into these tissues; and it is influenced, by, 2, the conditions present while this conversion is occurring. These views were originally put forward in a paper "On the Formation of the so-called Intercellular Substance of Cartilage, and of its relation to the so-called Cells, with Observations upon the Process of Ossification," published in the "Trans. of the Microscopical Society," No. XII., October, 1863.

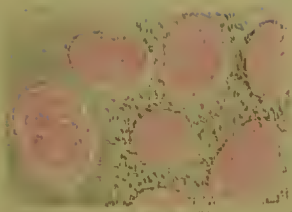
During the very early stages of development, *fibro-cartilage* and spongy cartilage could scarcely be distinguished from ordinary permanent cartilage, but later the texture might be almost mistaken for young fibrous tissue. In fig. 133, pl. XV., page 230, a good specimen of fibro-cartilage from the intervertebral discs of a fœtal kitten is represented. The bundles of fibrous tissue are already distinctly marked, but nothing like firm cartilage-matrix is yet formed. This appears at a later date. Of the masses of germinal matter seen in the specimen, which are now exactly alike, some at a later period produce cartilage, while others continue to give rise to fibrous tissue. It has been already shown that cartilage and fibrous tissue are continuous with one another and that the homogenuous or slightly granular formed material of the cartilage shades gradually into the fibrous tissue of the tendon, fig. 129, pl. XV.

Changes occurring in the Germinal Matter of fully formed Cartilage.—The formation of matrix or tissue continues even in adult cartilage. Although the entire mass may undergo no alteration in size, new tissue is produced to compensate for the shrinking and condensation, which the tissue undergoes as it advances in age. Slowly indeed are these changes carried on, because the "matrix" is very slightly permeable to fluids. But the germinal matter still has the *power* to grow rapidly, and it will do so if the matrix become more permeable, or if the access of the pabulum to the germinal matter is facilitated by artificial means. As in other cases the rapidity of the growth of germinal matter simply depends upon the supply of pabulum. Let a thread be passed through a healthy cartilage, so as to make artifically a channel by which the pabulum may reach the masses of germinal matter more quickly, and the operation will be very soon followed by the increase in size and division of the

masses of germinal matter. The formed material in their immediate neighbourhood will be softened, and may even be appropriated by them. This state of things continuing, pus may result, or the masses of germinal matter not multiplying so fast as is involved by this supposition, may give rise to the formation of a soft pulpy formed material, like that of embryonic cartilage at an early period of development. These changes cannot be explained by what is called "*irritation*," nor are the cells "*stimulated*" to take up more nutrient matter within a given period of time than in the normal state, but the alteration depends simply upon the restrictions to the access of the pabulum to the germinal matter having been to some extent removed.

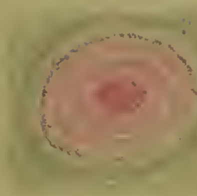
Fatty matter is very often deposited from the germinal matter of cartilage. In some cases, the cavity in the matrix of the cartilage seems to be entirely occupied by the oil globule or globules. In the cartilage of the ear of some of the smaller animals which are fat and well fed, the so-called cartilage cells appear to be occupied by globules of fat as large as those which are enclosed in the fat vesicle, pl. XV, fig. 132, p. 230. The process can hardly be regarded as morbid, unless the formation of adipose tissue itself is looked upon as pathological. In this as in many other cases, it is impossible to separate physiological from pathological operations. A similar change is not unfrequently seen in cases in which the cornea exhibits the arcus senilis, as was first pointed out by Mr. Edwin Canton, and often accompanies fatty degeneration of other tissues of the body. These phenomena are undoubtedly due to changes which must be considered morbid.

Fig. 134.



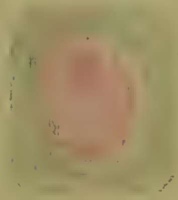
Very young cartilage. Frog. Oval masses of bioplasm separated by soft imperfectly formed intervening substance × 700.

Fig. 135.



Germinal matter about to undergo conversion into formed material. × 700. pp 220, 229, 230.

Fig. 136.



An older elementary part. Cartilage, frog, with recently formed cartilage and tissue × 700. p. 220.

Fig. 137.

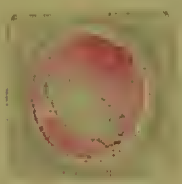
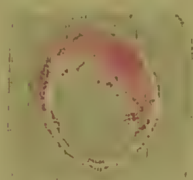
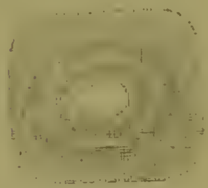


Fig. 138.



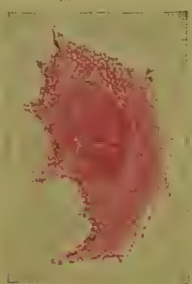
Elementary parts showing that not only does the bioplasm undergo conversion into cartilage at its external surface but that this alteration may occur as well in the central parts × 700. p. 230.

Fig. 139.



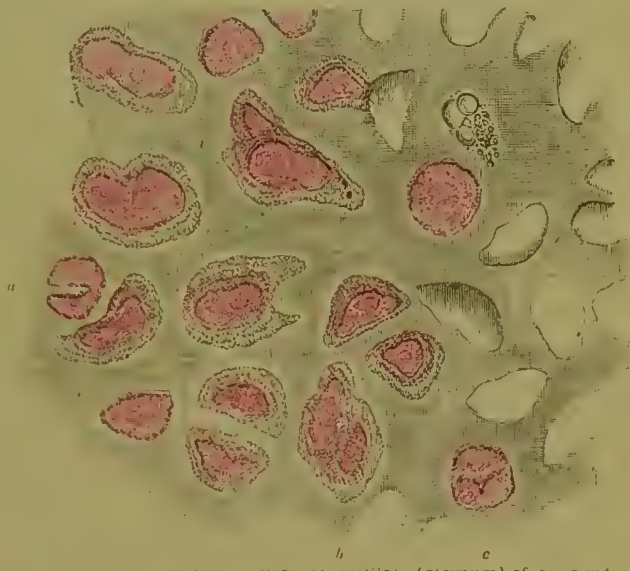
Space in matrix once occupied by bioplasm, nearly all having undergone conversion into matrix. × 700 p. 230,

Fig. 140.



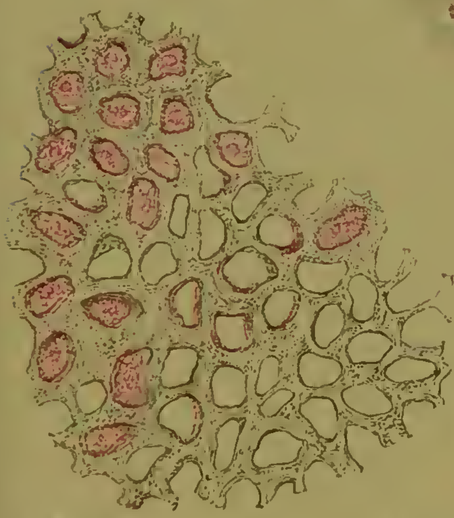
Young cartilage, kitten, showing the CONTINUITY OF THE GERMINAL MATTER WITH THE FORMED MATERIAL IN WHICH IT IS UNDERGOING CONVERSION. × 1800 p. 229.

Fig. 141.



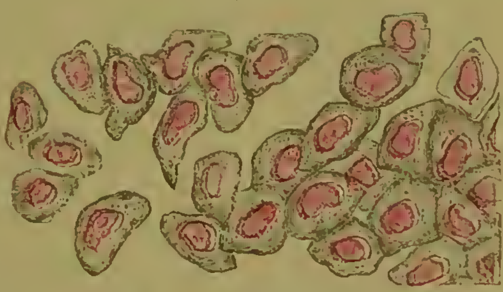
very thin section of cartilage (sternum) of a young newt, showing masses of germinal matter, some of which are dividing at *a*, *b*, *c*: with formed material which is continuous throughout as in young epithelium × 500. See Fig. 143. pp. 229, 231

Fig. 142.



Young epithelium from the deep layer of the conjunctiva (the membrane covering the front of the eye) of a girl showing the formed material continuous and not yet separated into portions corresponding to each mass of germinal matter. Here there are no separate "cells". This shows that tissues, like epithelium which exhibits a "cellular" character are not marked off from those supposed to exhibit an intercellular substance. This tissue might be described as consisting of "intercellular substance" at one time and of "cells" at another. See Fig. 143 × 500

Fig. 143.



Superficial or older cells, from the same specimen as Fig. 142, showing formed material belonging to each mass of germinal matter, giving rise to the appearance of separate cells × 500

[To face page 234

CHAPTER VI.

OF BONE OR OSSEOUS TISSUE.—CHEMICAL COMPOSITION.—COMPACT TISSUE AND CANCELLATED STRUCTURE.—OF LIVING AND DEAD BONE.—AN ELEMENTARY PART OF BONE.—OF THE LACUNÆ AND CANALICULI.—FORMATION OF LACUNÆ AND CANALICULI.—CANALICULI NOT PROCESSES OF A CELL.—ULTIMATE STRUCTURE OF OSSEOUS TISSUE.—VESSELS OF BONE: RELATION TO OSSEOUS TISSUE.—HAVERSIAN SYSTEMS AND RODS.—LAMELLÆ.—HAVERSIAN CANALS AND SPACES.—DR. SHARPEY'S PERFORATING FIBRES.—PERIOSTEUM AND MEDULLARY MEMBRANE.—MEDULLA OR MARROW OF BONE.—MYELOID CELLS.—NERVES OF BONE.—DEVELOPMENT OF BONE.—GROWTH OF A LONG BONE.—REPAIR OF BONE.—GROWTH OF GERMINAL MATTER OR BIOPLASM OF BONE.—INFLAMMATION OF BONE.—CARIES.—NECROSIS.

BONE differs from every other texture which has yet been brought under notice, in the important character that the formed material, matrix, or soft tissue, is impregnated with calcareous salts, which are intimately incorporated with it. A very firm unyielding tissue thus results, which, however, possesses a eertain degree of elasticity, and although hard and of great strength, is by no means brittle. It often withstands violent shocks without fraeture, and being for the most part covered with soft tissues is in a measure protected; for the skeleton (bony or cartilaginous) of the higher animals, is *internal;* it is clothed by the muscles and other soft parts. The first example of this arrangement is met with in the cephalopodous mollusks, in which certain cartilaginous plates are enclosed in the body of the animal, protecting certain parts of the nervous system. The skeleton of the lowest organized fishes, although mueh more extensive, is soft and yielding, and is placed but little above that of the animals just referred to. It is composed of cartilage, which, however, in arrangement of its several parts, approaches the bony skeleton of the higher classes.

Bone is the substanee employed to form the internal skeleton of the osseous fishes, of reptiles, birds, and mammalia. It

forms organs of support, or levers for motion, or it encloses cavities, affording protection to soft tissues and to organs of vital importance. In some members of the vertebrate series, bone is found associated with various tissues, as the skin, tendon, and certain forms of fibrous tissue, as the sclerotic coat of the eye.

To a superficial examination, bone presents the following properties: hardness, density, a whitish colour, opacity. An examination of its physical constitution will explain these characters.

Bone contains less water than most other tissues in the body; and exposure to air, even for a short time, removes much of the fluid by evaporation; to this, in part, may be attributed its hardness. It is easy to prove that bone consists of soft *organic tissue*, exhibiting structure, and *hard calcareous matter* deposited in its substance. These may be separated by a very simple process. The soft organic matter may be obtained by steeping a bone for some time in dilute hydrochloric acid (one part of acid to three of water), for this acid dissolves the calcareous salts, and leaves the tissue of the bone. The decalcified tissue is so soft, that a long bone treated in this way may be bent in any direction, or even tied in a knot. Yet every eminence, every minute canal, and even the slightest inequalities of the surface are as distinctly marked as they were before the action of the acid. Upon the addition of excess of ammonia to the acid solution, the calcareous salts may be precipitated in an insoluble form, and by applying appropriate tests, phosphates of lime and magnesia, a little carbonate of lime, with traces of fluoride of calcium, may be detected.

Again, the calcareous salts of the bone may be made evident by another process which causes the destruction of the organic matter. If a bone be subjected to a red heat in a crucible, it becomes charred and black; but if kept for some time at this high temperature, exposed to the air, the carbon is gradually burnt off, escaping as carbonic acid, while the calcareous salts remain behind in a pure state. If the process is conducted with care, although the bone shrinks a little, its form is unaltered, and every eminence and every hole is as distinct as in the recent bone, or in the bone treated with acid; but the cohesion between the earthy particles is extremely slight, so

that the least touch will destroy the continuity of the texture; a fact which obviously points to the animal matter as affording to bone its strength of cohesion.

Bone may also be deprived of its animal matter by long-continued boiling, under strong pressure, in a Papin's digester. The animal matter is extracted, in combination with water, in the form of *gelatine;* and the weight of the quantity which may thus be obtained will, owing to this union with water, exceed by three or four times that of the bone itself.

We subjoin the following process, by which the qualitative analysis of the inorganic matter of bone may be readily effected:—

The *earthy matters* are best examined by treating a portion of burnt bone with nitric acid, diluted with from four to six times its bulk of water; brisk effervescence ensues, proving the presence of *carbonic acid.* Filter the acid liquid after diluting it with water, and add solution of caustic ammonia as long as the precipitate at first formed continues to be redissolved by agitation; then add solution of acetate of lead till it no longer occasions any precipitate. The dense white precipitate thus produced consists of *phosphate of lead*, which melts before the blow-pipe, and on cooling assumes its characteristic crystalline structure. Through the solution, filtered from the phosphate of lead, pass a stream of sulphuretted hydrogen to remove the excess of lead; warm the liquid, to drive off the superfluous gas, and filter: then neutralize by ammonia, and add oxalate of ammonia as long as any precipitate occurs; abundance of *oxalate of lime* will fall as a white powder. Evaporate the filtered liquid to dryness; ignite the residue, and wash with hot water; the *magnesia* will be left behind in a pure form.

We shall see that in the formation of bone, the production of the soft tissue is *one process*, and the precipitation of lime salts from the fluid which permeates it, and their incorporation with the soft matrix, *another process.* The first cannot be brought about except by *vital actions.* The last is due to *chemical changes*, and can be, to a certain extent, imitated artificially. Soft bone tissue is formed in certain instances, but in consequence of the secondary process of calcification not having been completed, it remains perfectly soft and useless for the the purposes for which bone is wanted. In the formation and

growth of this tissue, we can therefore define with great precision the results of the vital processes, and distinguish these from the effects of the purely physico-chemical changes.

A certain proportion between the organic and inorganic constituents of bone is necessary to the due maintenance of its physical properties. To the earthy part it owes its hardness, its density, its little flexibility; but it is equally necessary for these properties that the animal portion shall be healthy, and in proper quantity; for the cohesion of the particles of the former is secured entirely by it. A due proportion of the animal part gives bone a certain degree of elasticity; and, were it not for the earthy matter, bones would be exceedingly flexible, as may be shown in a bone deprived of its calcareous matter by acid. Hence old bones, in which the animal matter is less abundant, as well as perhaps defective in quality, are more brittle than young ones, and the bones of old persons are more liable to fracture. But in the young, in whom the organic processes are active, and whose animal matter is fully adequate in quantity and quality to the wants of the system, the bones possess their due degree of flexibility, and hence in them fractures are less frequent; the cohesive force of the bones being sometimes so considerable, that they will bend to a great degree before yielding.

The following table from Schreger illustrates the relative proportions of the two constituents, at three periods of life, in 100 parts of bone :—

	Child.	Adult.	Old.
Animal matter	47·20 ..	20·18 ..	12·2
Earthy matter	48·48 ..	74·84 ..	84·1

or it may be stated in general terms, that in the child the earthy matter forms nearly one-half the weight of the bone, in the adult is is equal to four-fifths, and in the old subject to seven-eighths; a conclusion agreeing in the main with that drawn from the analyses of Davy, Bostock, Hatchett, and others.

It had long been known that certain bones of the body contained these constituents in other proportions than those named; for example, the petrous portion of the temporal bone had been shown by Davy to owe its stony hardness to an exceptionally large proportion of earthy matter. But Dr. G. O. Rees has

pointed out some interesting particulars as to the relative proportions of these elements in the composition of different bones. The long bones of the extremities have, according to Dr. Rees' analyses, more earthy matter than the bones of the trunk. The bones of the upper extremity have a larger proportion of the same material than those of the corresponding bones in the lower; the humerus has more than the radius and ulna; the femur more than the tibia and fibula; while the bones of the fore-arm, as well as those of the leg, are respectively alike in constitution. The vertebræ, ribs, and clavicles are similarly constituted. The ilium has more earthy matter than the scapula or sternum; the bones of the head have more of this material than those of the trunk.

In the fœtus the same law prevails as regards the relative quantity of the earthy matter, excepting that the long bones, and the cranial bones, do not contain the excess of earthy matter which characterizes them in the adult.

The diseased state, called Rickets, so common in the children of scrofulous parents, and in the ill-nourished ones of the lower orders, consists in a deficient deposit of earthy matter; the animal matter being probably of an unhealthy quality. In this disease the bones are so flexible, that they may bend under the weight that they are called on to support, or under the action of the muscles. The lower extremities exhibit deformity first, and to the greatest degree, and the direction in which they become bent is evidently influenced by the superimposed weight; the bend almost always appears as an aggravation of the natural curves of the bones. The rickety femur has always its convexity directed forwards; the tibia is convex forwards and outwards, and the fibula follows the same direction. When the nutritive powers of the system are fully restored, the deposition of earthy matter goes on in its healthy proportion, the animal matter becomes healthy, and the bones acquire their due degree of strength and hardness. In the tibia of a rickety child, Dr. Davy found, in 100 parts, 74 parts animal matter, and 26 earthy; and Dr. Bostock found in the vertebra of a similar subject 79·75 animal, and 20·25 earthy.

The brittleness of the bones in old age is due to an opposite cause, namely, the gradual removal of animal matter, so that

the earthy matter unduly preponderates. But this state cannot be looked upon as morbid; it is the natural result of the feeble condition of the powers of nutrition, and the drying up and hardening of the tissues which ensue as age advances; and it will vary in different individuals, according to the original strength of constitution of each, and according to the freedom from exposure to debilitating influences.

In that rare form of disease, known as *mollities ossium*, which occurs in adults, the bones are sometimes so soft that they may be indented by pressure with the finger. The nutritive processes concerned in the formation of the bone seem affected, for not only is the osseous tissue deficient in earthy material, but the animal matter is not in a healthy state, and in many instances fatty matter is present in unusual proportion. In these cases, the pathology of which is very obscure, earthy phosphates are often excreted in the urine in abnormal quantity. Analyses of the urine in two different cases are given below.*

Analyses.	In 100 parts of solids.		In 100 parts of solids.	
Water	971·9	—	960·88	—
Solid matter	28·1	100·00	39·12	100·00
Urea	5·0	17·7	—	—
Extractives	10·22	36·3	—	—
Fixed salts	12·88	45·81	5·25	13·42
Earthy phosphates precipitated by ammonia	1·185	4·21	·4	1·02
Alkaline phosphates precipitated by sulph. magnesia and ammonia	1 13	4·21	1·3	3·32
Triple phosphates filtered from the urine	—	—	—	—

The large proportion of earthy phosphate in these analyses is a very interesting fact. In the first, the earthy actually exceeds the alkaline phosphate; and, in the second, it is nearly equal to it. In healthy urine the alkaline phosphate usually amounts to from ten to fifteen times as much as the earthy phosphate. The inorganic salts generally, in these specimens of urine, were in considerable excess.

Bones possess a remarkable power of resisting decomposition. Even the animal part seems to acquire this power

* See "On Kidney Diseases, Urinary Deposits and Calculous Disorders," by Lionel S. Beale, M.B., F.R.S. Third Edition, page 217.

through its combination with the earthy. This is manifest from analysing bones which have been long kept, or fossil bones. Cuvier states that the latter bones exhibit a considerable cartilaginous portion; and Bichat found that clavicles, which had been exposed for ten years to the wind and rain at the cemetery of Clamart, presented, under the action of acid, an abundant cartilaginous basis. In an old Roman frontal bone, dug up from Pompeii, Dr. Davy found 35·5 animal parts, and 64·5 earthy; and in a tooth of the mammoth, 30·5 animal, and 69·5 earthy.

Chemical Composition.—The animal part of bone consists of cartilage basis, with vessels, medullary membrance, and fat. The former is readily convertible into gelatine, according to Berzelius, after three hours' boiling; and, when this has been removed, there remain only four grains out of 100, which may be considered to have been composed of blood-vessels.

The earthy part of bone consists of phosphate and carbonate of lime, with a small quantity of phosphate and carbonate of magnesia. The phosphate of lime forms the principal portion of the earthy part: in 100 parts of bone, Berzelius found 51·04 of this salt. It was discovered by Gahn, and the discovery announced by Scheele, that bone-earth consisted of "phosphoric acid and lime." According to Berzelius, the phosphate consists of eight atoms of lime and three atoms of phosphoric acid; but Mitscherlich regards it as composed of three atoms of lime with one of phosphoric acid (a tribasic salt). It may be formed artificially by dropping chloride of calcium into a solution of phosphate of soda. It appears as a gelatinous precipitate, which does not crystallise, and is readily soluble in acids.

The existence of fluoride of calcium in bone was announced many years ago by Berzelius, who found as much as 2 per cent. According to Berzelius, the following represents the composition of bone. The accuracy of these results have been confirmed more recently by Mr. Middleton (*Phil.Mag.* vol. xxv., p. 18).

Animal matter	33·30
Earthy matter	66·70
Phosphate of lime	51·04
Carbonate of lime	11·30
Fluoride of calcium	2·00
Magnesia	1·16
Soda and chloride of calcium	1·20

Compact Tissue and Cancellated Structure.—In examining a section of almost any bone, we observe two varieties of osseous substance: the one *dense, firm, compact, always situated on the exterior of the bone,* either as a thin layer, or as a dense, thick structure possessed of great strength; the other *loose, reticular, spongy,* arranged so as to exhibit spaces or cells, which communicate freely with each other, and which, being called *cancelli,* give to this kind of osseous tissue the name *cancellated.* These cancelli are formed by an interlacement of numerous bony fibres and laminæ, which, although to a superficial observation exhibiting an indefinite arrangement, have nevertheless, in those bones which have to support weight, a more or less perpendicular direction. The cancellated structure of bone is always situated in its interior, enclosed and protected by the compact tissue.

Fig. 144.

Vertical section of the upper end of the Femur, showing the cancellated and compact tissues.

The relative situation of these varieties may be well seen in a vertical section of one of the long bones (fig. 144). At the *extremities,* the cancellated texture is accumulated, invested by a thin lamella of compact tissue, giving expansion and lightness to those parts of the bone. In the intermediate portion, or *shaft,* the compact tissue is highly developed, affording great strength in the situation where that quality is the most needed.

The compact external surface of bone (except on its articular aspects) is covered by a firm tough membrane, termed the *periosteum,* which, like the perichondrium investing cartilage, consists of white fibrous tissue, densely interwoven in all directions (see page 269). The cancelli are filled with fat, or *medulla,* the marrow of bone. They are lined by a delicate membrane, called the *medullary membrane,* which serves to

support the fat. In the shaft of the long bones the medulla is contained, not in ordinary cells, but in one great canal, which occupies the centre of the shaft, the *medullary canal*. Here the *medullary membrane* lines the compact tissue that forms the wall of the cavity.

Both the periosteum and the medullary membrane adhere intimately to the bone. Both are abundantly supplied with blood-vessels, which, after ramifying upon them, send numerous branches into the bone. These membranes are of great importance to the nutrition of the bone, inasmuch as they support its nutrient vessels; and, if either of them be destroyed to any great extent, the part in contact with them necessarily perishes: and they not only cover the outer and inner surfaces of the bone, but *also send processes, along with the vessels, into minute canals traversing the compact tissue*, and are, through the medium of these, rendered continuous with one another. When the periosteum or medullary membrane is torn away from the surface of a fresh bone, the vessels may be seen very readily passing from the under surface of the membrane into the tiny channels (Haversian canals) which pass obliquely into the compact tissue. The vessels of the bone ramify throughout its substance, and if they have been injected previously to the removal of the calcareous matter by the action of acid, they will be distinctly seen ramifying through the semi-transparent animal substance. A preparation of this kind dried, and afterwards preserved in spirits of turpentine, serves beautifully to exhibit the disposition of the vessels in bone.

Of living bone and of dried dead bone.—The authors of many manuals and treatises on minute anatomy have described the structure not of *living* or *recently dead* bone, but of bone which has been *dead for a long time and has undergone desiccation.* The student is thus led to acquire a notion of the structure of bone as imperfect and incorrect as would be that which he would form of the structure of skin, nerve, or muscle, were he to examine dried specimens of these tissues only. We desire to learn what is the structure of tissues, and how they live and grow and decay in the living body; but the structure of bone and teeth has been described, not as it may be demonstrated in these tissues when they are fresh, but only as it appears after

they have been altered by *drying*, and after they have been completely deprived of their *living matter*.

An elementary part of dead dried bone.—An elementary part of fully-formed *dead* and *dried bone* consists of a *space* (*lacuna*), occupied in the recent state with germinal matter, with a certain portion of hard osseous tissue which is traversed by numerous pores or channels (*canaliculi*) passing from one little space (*lacuna*) in a tortuous manner to adjacent lacunæ, fig. 145.

An elementary part of living bone.—An elementary part of *fully-formed living bone* consists of a mass of germinal matter, surrounded on all sides by, and continuous with, a thin layer of soft formed material, which passes uninterruptedly into the hard calcified formed material (*matrix or intercellular substance of authors*) pl. XVIII, fig. 164. This hard material is in the fully formed bone penetrated everywhere by very fine channels (*canaliculi*) through which the nutrient fluid passes towards the masses of germinal matter; for, as the hard material in its fully formed state is almost impermeable, nutrient fluid could not reach the germinal matter were it not for these little canals or canaliculi in its substance.

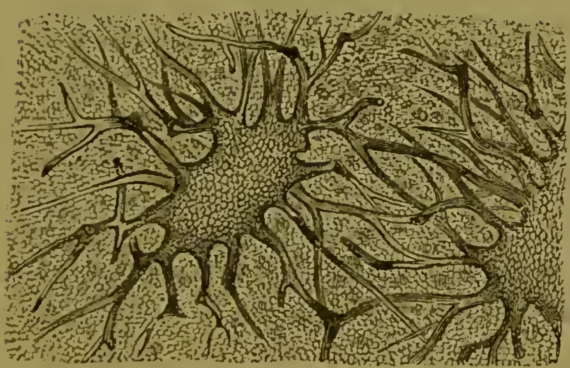
An elementary part of every kind of bone at *a very early period of its formation*, consists of a mass of germinal matter, surrounded by a certain proportion of granular, homogeneous or more or less fibrous formed material. This last becomes the seat of deposition of calcareous matter, which proceeds in a direction from *without inwards*. The formation of the canaliculi takes place in the same direction. One of us (L. S. B.) has shown, in opposition to the generally received opinion, that the formation of these tubes commences not at a point nearest to the germinal matter or "cell," as has been repeatedly stated, but at a distance from it. See pages 249, 254.

The difference between *dead bone* and *living bone* is simply this: in the first, *formation* of tissue has everywhere ceased; while in the last, it is still proceeding, and around each mass of bioplasm the *production* of matrix and the deposition of calcareous salts in the matrix already formed is going on. These changes may proceed very slowly, but in all living bone they are taking place. The only matter in a living bone which is actually *alive* is that which is ordinarily termed the "*nucleus*"

or the "*bone cell*" in the space or lacuna, and which is here spoken of as the germinal or living matter or *bioplasm.* Plates XVII to XIX. The fully-formed osseous tissue around, on the other hand, is to all intents and purposes, as devoid of life while the bone yet remains a part of the living body, as after it has been removed, or after the body has died. This small mass of germinal matter, perhaps not more than one-twentieth of the bulk of the proportion of bone tissue which belongs to it, alone possesses active powers. This only can *grow* and give rise to the *formation of matrix.* Bone cannot *produce bone* any more than *tendon* can give rise to *tendon* or *muscle* form *contractile tissue*, but the *germinal matter* or bioplasm only is instrumental in the formation of every one of these tissues, and without this the production of tissue is impossible.

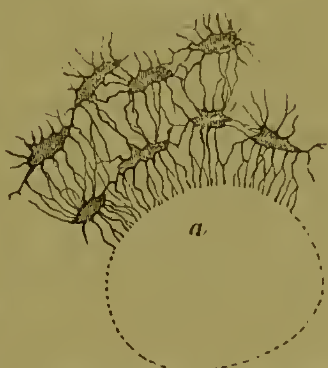
Of the Lacunæ and Canaliculi.—All the osseous tissue with which the human anatomist is concerned is of such bulk as to contain the series of pores and cavities already alluded to for the conveyance of fluid. These *pores* always advance into the bone from open orifices on its vascular surface. They are arranged in sets, each of which, after anastomosing with neighbouring ones, discharges itself into a small cavity or *lacuna*, in

Fig. 145.



Two lacunæ of osseous tissue, seen on their surfaces, showing the disposition of their pores. The granular aspect of the tissue both on their walls and around them is well represented.—Magnified 1200 diameters. Drawn from a preparation of the cancelli of the Femur made by Mr. Tomes.

Fig. 146.



Transverse section of a part of the bone surrounding an Haversian canal, showing the pores commencing at the surface, *a*, anastomosing and passing from cavity to cavity.—Magnified about 300 diameters From a preparation made by Mr. Tomes.

which its individual pores coalesce. From the sides of this lacuna other pores pass off to similar cavities in the vicinity, and, from its opposite surface, others proceed to penetrate still deeper into the tissue. These pour themselves into another lacuna, or

divide themselves between two or three, which are connected in like manner by lateral channels, fig. 146. From these again pass others; and so on, until the whole substance of the bone is perforated by them, so that no particle of the hard osseous tissue is distant more than the $\frac{1}{10000}$ of an inch from one of these fluid carrying *canaliculi*.

When this beautiful system of microscopic pores and cavities was first seen, it was not recognized as such. The lacunæ were imagined to be solid *corpuscles* (a name still commonly applied to them), and the lines radiating from them to be branching threads of the earthy constituent of bone. In the dry bone the lacunæ and canaliculi are both filled with air, and in consequence of the great difference in refractive power between the air and the transparent bone tissue, the light is so bent out of its course in passing from one medium into the other, that the cavities and tubes appear *black*, as a small air bubble in water appears like a mass of dark solid matter. It was this solid appearance which led Purkinje, their discoverer, to call them "bone corpuscles." They may be proved in many ways, however, to be real excavations in the tissue. With a sufficiently high power their opposite walls can be distinctly seen, as well as their hollow interior; but the most conclusive evidence lies in our being able to fill them with fluid. If a dry section of bone, in which they are very apparent, be moistened with oil of turpentine while in the field of the microscope, the course of this penetrating material can be witnessed, as it advances into the tissue. It is seen to run quickly along the pores from the Haversian canals, and from the surface of the specimen, where they have been cut across. Having entered a lacuna, it suddenly extends along the pores radiating from it, and, through these, reaches other lacunæ; rendering the tissue transparent by filling up its vacuities. In parts where air has previously occupied the vacant spaces, and the turpentine cannot displace it, the characteristic appearance of minute bubbles is often present. The refractive power of the turpentine so nearly corresponds to that of the osseous tissue, that the whole section appears homogeneous, and it is only with great difficulty that either lacunæ or canaliculi can be discerned: so different are the appearances produced by different processes of examination in the same dead dried tissue.

The *lacunæ* of osseous tissue, if examined extensively in the vertebrate class, are found of very various shapes: sometimes scarcely to be distinguished from the pores, of which they are simple fusiform dilatations; at other times large and bulky, and forming the point of junction of a great multitude of pores. Mr. Tomes has allowed us to represent the principal varieties which he has met with in the human subject; and some remarkable ones from the lower animals are appended (fig. 147.)

Fig. 147.

Form of various lacunæ, and their pores:—*a*. Simple irregular cavities, without pores; from an ossification of the pleura: *b*. from healthy bone of the human subject. *b′*. One of the outer lacunæ of an Haversian system, with the pores all bending down towards the H canal. *c*. Other forms from human bone, showing the lateral connecting pores.

d. From the boa. External lacunæ of an H system, with unusually large pores dipping towards the vascular surface. *d′*. Cavity intermediate between a lacuna and a pore. *e*. Another variety from the same reptile.—From Mr. Tomes.

But though varieties are occasionally met with, yet, in the true bone of man and mammalia, the lacunæ possess a very constant form; being somewhat oval and more or less flattened on their opposite surfaces. The two surfaces look respectively to and from the nearest surface of the tissue and meet in a thin edge. As pores pass off equally from all parts of the lacunæ, it follows that by far the greater number pass to or from the surface of the bone; an arrangement admirably adapted for the transmission of the nutritious fluids which transude through the walls of the vessels. In fig. 145 the lacunæ are seen on their surface; in fig. 146, on their upper edge.

The lacunæ have an average length of $\frac{1}{1800}$ of an inch, and they are usually about half as wide, and one-third as thick.

The diameter of the pores is from $\frac{1}{20000}$ to $\frac{1}{12000}$ of an inch.

In growing bone the canaliculi are probably occupied by the original matrix of the cartilage or organic texture, but in bone which has ceased to grow the organic material contracts and becomes dry. The canaliculi are in that case true tubes, without any soft material occupying their cavity. Air is sometimes found in the lacunæ and canaliculi even of recent bone, pl. XIX, fig. 184; and there is reason to think that during life this is the case in certain parts where the osseous tissue is fully formed and old.

The osseous tissue thus studded by thousands of flattened lacunæ, which lie for the most part in planes parallel to the surface, has a decided disposition to split up into *laminæ*, following the same direction. This is more evident in the bones of old persons, and may be promoted by maceration in dilute acid. It is most apparent where the mass of material between two vascular surfaces is great, and the series of lacunæ numerous. This lamellated structure, there is reason to think, is due to the manner in which the development and growth of the osseous tissue proceed. *See* page. 265.

Of the formation of Lacunæ and Canaliculi.—The investigation of the formation of lacunæ and canaliculi in growing bone presents difficulties, and many of the conclusions which have been arrived at upon the matter have been based rather upon hypothesis than upon actual observation. It is remarkable that some of the views entertained upon this subject are opposed to actual facts which may be readily demonstrated by a careful anatomist. It is desirable, therefore, that we should study the changes which may be observed to take place in simple cartilage during its conversion into bone. Now, in the frog, the phenomena occur much more slowly than in mammalia, while the elements of the tissue are upon a larger scale, and in properly prepared specimens we can trace the various stages through which the cartilage tissue passes in its conversion into bone with great accuracy. If the reader will attentively examine the figures referred to, a very short description will enable him to grasp the actual facts. Fig. 148, pl. XVII, represents a very thin section of cartilage at the edge of one of the cranial bones of a common frog, not quite

full grown, prior to the commencement of ossification. The germinal or living matter and the *matrix* or *cartilaginous tissue* are well seen. The drawing represented in fig. 149 was copied from a part of the tissue further inwards, or in other words, nearer to the bone tissue already formed. Here globules of earthy matter may be seen deposited in the matrix so as to form imperfect rings around the cartilage cells. The calcareous matter it will be observed has been deposited in the matrix (formed material) at a point midway between adjacent masses of germinal matter, that is, in the *oldest portion of the formed material* of the cartilage. The deposition gradually proceeds *from without, inwards.* See also figs. 163, 164, pl. XVIII. This is invariably the case in every form of bone. While this process is going on, the outer part of each mass of germinal matter gradually undergoes conversion into matrix, which in its turn becomes impregnated with calcareous matter.

The next stage is seen in fig. 150, where the calcareous globules have encroached still nearer to the bioplasm, and in figs. 151 and 153 the incorporation of the earthy matter with the organic matrix is almost complete. Distinct globules are no longer to be seen, and the tissue is fast assuming the characters of fully formed bone. The calcareous matter is precipitated in distinct globules, which are well seen in the drawings, and these may be detected, with the aid of very high powers, in the formation of the osseous tissue of mammalia.

Indeed, for some time after the first deposition of the calcareous matter in the formed material, the very thin fragments of the bone, which may be torn away, and exhibit the appearance of fibres (a fact pointed out many years ago by Dr. Sharpey), show many minute globules, pl. XVII, fig. 154, but slowly the calcareous matter becomes more homogeneous, in consequence, probably, of changes occurring in its substance, and its more perfect incorporation with the organic matrix; and ultimately the hard mass appears even in texture, uniformly transparent, and as has been already stated, penetrated everywhere by minute canals.

During the progress of the changes above described nutrient material and calcareous matter in solution have been continually flowing towards the germinal matter, and fluid deprived of its elements of nutrition and earthy salts, in the opposite

direction. The soft matrix of the cartilage is everywhere permeated by these fluids; but as its calcification proceeds, the area of the tissue, which is permeable, becomes more and more restricted, until at last the only permeable texture which remains in the bone is that thin portion which lies between the globules of calcareous matter. These lines being continually traversed by currents of fluid the deposition of calcareous matter is prevented and free channels for the conveyance of the nutrient fluids are thus retained, pl. XVII, fig. 153.

These tubes or channels are therefore the altered spaces which are left between the calcareous globules originally deposited. They were at first triangular in outline, but gradually they have become altered by the filling up of the angles, until at last they become pores, the section of which is nearly circular, fig. 164, at *a*, pl. XVIII.

The views here advocated accord more nearly with the teachings of Henle, who compared the formation of the lacunæ to the changes which occur in the walls of certain vegetable cells through the secondary deposits of which pores are left (pl. III, p. 84, fig. 28), than with those of any other observer.

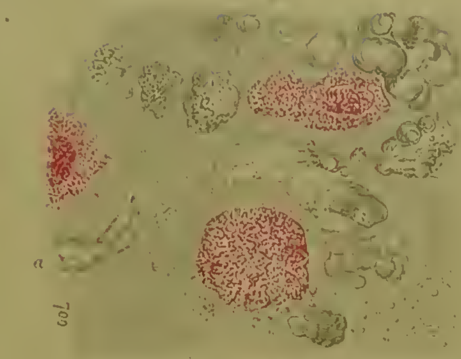
Thus, the deposition of the calcareous matter is truly a physico-chemical operation, but the formation of the matrix cannot be thus explained nor can the precise seat of commencement of the deposit, and its gradual encroachment towards a centre, be thus accounted for. Mr. Rainey* has described the phenomenon as if it were purely physical, because he found that calcareous particles could be deposited in a *previously formed* matrix artificially, fig. 158, pl. XVIII. Now, Mr. Rainey's drawing, fig. 160, though fairly representing the arrangement of a portion of dead bone, gives no idea of the manner in which the tissue is formed, for the most important element, that which is never absent in growing bone—that without which the formation of such a tissue is impossible, has been ignored, as if it did not exist. Mr. Rainey has entirely omitted the *germinal or living matter*, or *bioplasm*, which is to be seen in *every specimen of actually growing bone, shell, and every other tissue.* In every one of the spaces represented in Mr. Rainey's figure a mass of germinal or living matter, or "nucleus," existed when the specimen was fresh. *See* figs. 159, 163, 164, pl. XVIII.

* "On the Mode of Formation of Shells of Animals, of Bone," &c.

Fig. 148.

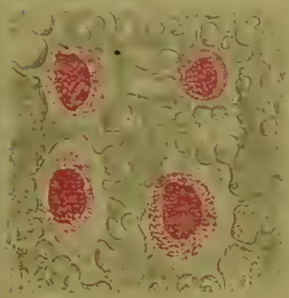
Cartilage of the temporal bone of an adult frog prior to ossification, showing bioplasm and formed material. × 700. p. 248.

Fig. 149.



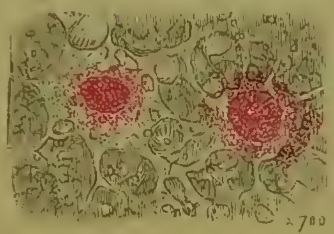
Another portion of the cartilage near ossifying surface, from the same specimen as Fig. 148, showing globules of calcareous matter, *a*, deposited in matrix. p. 249.

Fig. 150.



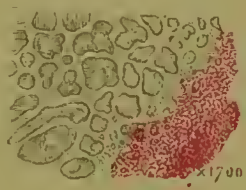
A further stage of the same process as that represented in Fig. 149. p. 249.

Fig. 151.



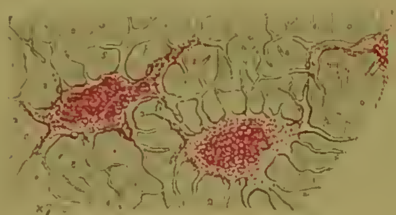
Two lacunæ from the frontal bone of the adult frog in process of formation. The mode of formation of canaliculi is shown. p. 249.

Fig. 152.



One third of the inner part of the wall of a fully-formed lacuna, magnified 1,700 diameters. p. 250.

Fig. 153.



Two recently formed lacunæ from the frontal bone of the frog. As the lacunæ advance in age, the canaliculi become narrower. × 700. p. 250.

Fig. 154.

A fragment of osseous tissue torn from perfectly formed bone, from the frog. The canalicular tubes between the particles of calcareous matter are well seen. × 1,700. pp. 249, 250.

Fig. 155.

Two lacunæ from the femur of the kitten at birth. × 700. p. 250.

Fig. 156.

Two lacunæ in the recently formed bone of the femur of the kitten. The bioplasts have undergone division. p. 287.

Fig. 157.

A small lacuna kitten. Almost perfectly formed. Magnified 1,700 diameters. p. 250.

$\frac{1}{1000}$ of an inch — × 700.

— × 1,700.

L. S. B., 1881.]

[To face page 250.

If the growing bone of any animal be examined, after having been properly prepared with carmine fluid, the masses of bioplasm will be demonstrated without difficulty in the lacunal spaces. The fact of the presence of germinal matter or bioplasm in the lacunæ of fully formed bone has however been generally admitted by anatomists since 1850. Under the name of "nucleus" the bioplasm had been observed in the lacunæ of many specimens of osseous tissue, and Tomes and De Morgan demonstrated indications of these bodies in the lacunæ of fossil bone, in their paper published in the Phil. Trans. for 1853.

The masses of bioplasm are as necessary to the production of bone as they are to the formation of every other tissue. They are not directly concerned in the precipitation of the calcareous matter, but in their absence the production of matrix would be impossible. It is alone by the instrumentality of these masses of bioplasm that the regular circulation of fluids holding in solution the calcareous salts, is maintained throughout every period of bone formation. By this process the regularity in the formation of osseous tissue, which is so remarkable, is secured. *See* pl. XVII.

It is desirable in this place to refer briefly to the views generally entertained by recognized authorities concerning the formation of lacunæ and canaliculi of bone.

The views of Kölliker and Virchow.—Kölliker considers that the *capsule* of the cartilage cell and the intercellular matrix become impregnated with calcareous matter, while the granular cell corresponding to the primordial utricle of the vegetable cell, remains within unaltered. He thinks that the canaliculi extend through the matrix by resorption.

Virchow says bone contains, "in an apparently altogether homogeneous basis-substance, peculiar stellate bone-cells distributed in a very regular manner." According to this view it is maintained that the matrix is formed as a true *intercellular* substance, while from the "cells" it is supposed that processes *grow out*, and that these gradually make their way through the matrix and anastomose with corresponding processes from neighbouring cells. The "lacuna" is said to be occupied by a "cell" with stellate processes which pass into the canaliculi.*

* In the following note, copied from page 417 of Dr. Chance's translation, Vir-

There are few points in minute anatomy upon which such different views have been advanced as the one under consideration, for observers differ not only in the explanations and opinions they have put forward, but there are irreconcilable differences regarding their statements of fact. To assert that the cells throw out processes, is merely fanciful, for there are no facts whatever to justify such a statement. Although it has been repeatedly stated that the bone "cell" with its canalicular prolongations may be actually detached from the matrix into which its processes have bored their way, we have never seen any specimens which appear to us to justify such an inference, while we have utterly failed in every attempt to prepare specimens which would lead us to infer the existence of the slightest grounds for such a conclusion.

With regard to Virchow's view, it may be remarked that although it is true that in certain cases in which the bioplasm or germinal matter is more or less stellate, the so-called *processes* project a very short distance from the mass, they *never*, as far as can be ascertained, *correspond* in number with the canaliculi which exist in the fully formed bone, the latter being twice as numerous as the processes in question. Almost any form of bioplasm may exhibit this stellate appearance, but it has nothing whatever to do with the formation of the canali-

chow expresses himself very clearly as to the manner in which the supposed processes are formed from cells:—"The cartilage cells (and the same holds good of the marrow cells) during ossification throw out processes (become jagged) in the same way that connective tissue corpuscles, which are also originally round, do, both physiologically and pathologically. These processes, which in the case of the cartilage cells are generally formed after, but in that of the marrow cells frequently before, calcification has taken place, *bore* their way into the intercellular substance, like *the villi of the chorion do into the mucous membrane and into the vessels of the uterus*, or like the Pacchionian granulations (glands) of pia mater of the brain into (and occasionally *through*) the calvarium." Again, "the cells which thus result from the proliferation of the periosteal corpuscles are converted into bone corpuscles exactly in the way I described when speaking of the marrow. In the neighbourhood of the surface of the bone the intercellular substance grows dense and becomes almost cartilaginous, the cells *throw out processes*, *become stellate*, and at last the calcification of the intercellular substance ensues." This view of the formation of the canaliculi will be understood by reference to figs. 161, 162, pl. XVIII, in which the processes of the cell are represented as "boring" their way through the already calcified tissue. In fact, however, canaliculi exist long before the formation of the calcified tissue has taken place.

culi in bone *for that part of the canaliculus nearest to the lacuna is the last that is formed*, whereas if the canaliculus were a process of the bioplasm, that portion nearest to the bioplasm must be first developed.

In cases in which a portion of a lacuna with part of its canaliculi are detached from bone tissue which has been decalcified, it is probable that the circumstance is correctly explained as follows :—The inmost layer of tissue constituting the wall of the lacuna and of its canaliculi differs in consistence and resisting property from that which is external; not that this tissue is developed separately from the general mass of the bone texture. Its greater hardness is probably due to its very slow formation as in the case of the so-called *wall* of the dentinal tube which affords another instance of the same sort of artificial distinction of texture, and which has led to a similar view concerning its formation as a texture distinct from the so-called "intertubular tissue."

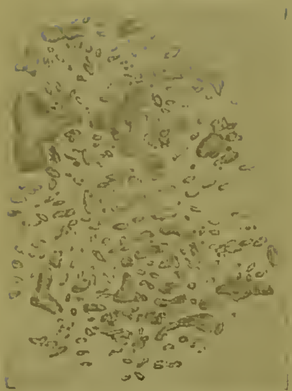
The size of the lacuna and the diameter of the tubes of the canaliculi *diminish* as the formation of the osseous tissue advances towards its mature state. How then can the *large* "cell-wall" of the *young* lacuna and of the wide canaliculi be the *very much smaller* "cell-wall" of the same lacuna and narrower canaliculi of the fully-formed tissue? But it is evident on other grounds that the views under examination have resulted from very artificial notions concerning the structure and growth of connective tissue, and these have themselves been based upon erroneous observation, and the belief in a structural analogy between bone and connective tissues, which exist only in the imagination.

*Canaliculi not processes of a Cell.**—"Although many observers have described and somewhat faintly expressed in their drawings the growth of the processes of the cell above referred to, all agree that they are most difficult to see in healthy growing bone. My own observations compel me to dissent from the statements generally made with regard to these processes. As far as I have been able to see, neither the cartilage cell, nor the medullary cell, nor the periosteal cell, nor indeed

* The observations in this paragraph were first published in my Lectures on the Tissues, in 1861. [L.S.B.] See also "Archives of Medicine," No. XVII. 1870.

any cell in the organism becomes stellate by the 'shooting-out process.' That cartilage and the other bioplasts or 'cells' may become angular is perfectly true, and that a few little projections may be seen from different parts of their surface is also true, but these projections and angles have nothing to do with the formation of canaliculi, *nor do they correspond to them in number*. The appearance is exceptional instead of being constant, and a *lacuna with numerous canaliculi* may be produced without the *existence of an angular cell at all.* The mass of bioplasm is *oval* from the period when it first existed as a separate object to the time of its enclosure in the lacuna, figs. 163 and 164, pl. XVIII. Into each lacuna forty or fifty or more canaliculi open, and these communicate with those of adjacent lacunæ. Surely, if these were formed in the manner described we ought to be able to demonstrate growing diverticula during the formation of the lacunæ, but nothing of the sort has been seen, and the warmest advocates of the theory have only been able to observe a very faint indication of the arrangement which they believe actually exists. Their drawings only show these processes projecting a very short distance from the cells, and no one, I believe, pretends to have seen processes from two neighbouring cells in process of communicating with each other, as shown in the fanciful explanatory drawing in fig. 161, pl. XVIII. I would ask, why, if the tubes grow centrifugally from the cells, they do not pursue the shortest route and pass in *straight lines?* By what force of attraction do the opposite tubes come into contact, and how is the barrier interposed between the two dissolved? But the impossibility of such a theory is shown in this way. Its advocates only pretend to account for the structure of the fully-formed bone, and do not attempt to explain by their theory the changes through which the tissue passes during the earlier periods of its formation. It is not only very difficult to conceive such channels formed by an out-growth, but it is inconsistent with what is generally observed. The tissue requires channels for the transmission of nutrient matter *during its formation,* just as much as after its formation is complete. The portion of the canaliculus which is first formed is that which is most *distant from*, not that which is nearest *to* the lacuna and its contents. The formation of of canaliculi takes place in a direction *towards* and not

Fig. 158.



Deposition of calcareous matter in the matrix of cartilage. After Mr. Rainey. The bioplasm is omitted. p. 250.

Fig. 159.

[illegible] which the calcareous particles are deposited and towards which currents of nutrient fluid converge. In Figs 158 and 160 a bioplast should be represented in every space. p. 250.

Fig. 160.

"Bone cells," after Mr Rainey. These are supposed to be formed without any bioplasm in the central spaces. p. 250.

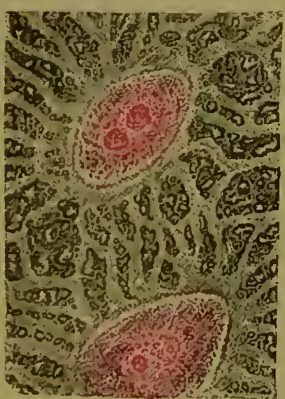
Fig. 161.

Diagrammatic representation of the imaginary "bone cells" supposed to exist; and their processes which are supposed to "bore their way" through the already formed bone tissue. p. 252.

Fig. 162.

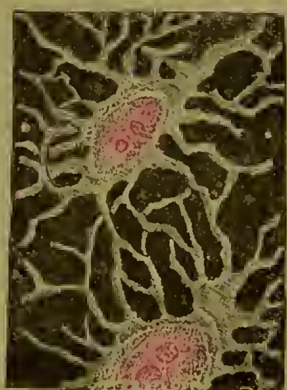
Diagrammatic representation of fully formed bone, showing the supposed "bone cells" with their processes which are now supposed to have bored through the bone and to have united with the processes of contiguous cells. p. 252.

Fig. 163.



Two bioplasts of bone with imperfectly formed lacunæ and canaliculi. These are left during the deposition of calcareous matter in the previously formed matrix. p. 254.

Fig. 164.



A further stage of the process represented in Fig 163. The tissue is now bone. The only matrix left uncalcified is that which corresponds to the canaliculi. The bioplasts have become smaller and now lie in spaces or lacunæ. p. 254.

[To face page 254.

from the bioplasm of the tissue—the so-called 'bone-cell' or 'nucleus.'" Figs. 150 to 155, pl. XVII.

If the canaliculi were formed as supposed it is quite impossible that every observer should have failed to see the prolongations of the cell undergoing development and coalescing with those of neighbouring cells. The extremities of these tubes which were gradually extending through the matrix would be rounded, as represented in pl. XVIII, fig. 161, and would contain germinal matter which would absorb the solid matrix, and thus the tube would extend through its substance, fig. 162. No such appearance has ever been seen. The canaliculi are no more processes of the cell which *bore their way* through the hard material than the canals which are left in the masses of secondary deposits in the hard walls of certain vegetable cells are processes pushed out from the germinal matter in the centre of the cell.

It may be said that the growing matter extending from a spore of mildew "bores" its way into the soft material, at the expense of which it grows, but in this case the soft material is clearly appropriated by the mildew, and becomes converted into the germinal matter of the plant. This process, and the conditions under which it occurs, are totally different from those which obtain in the case under consideration.

No stellate "*corpuscle*" has been found in bone, but the stellate appearance of the lacuna, with its radiating canaliculi has resulted from the circumstance that the calcareous matter has been deposited in the matrix in such a manner as to *leave intervals* arranged in a more or less stellate manner, as has been explained.

There is, however, room for some difference of opinion with regard to the *contents* of the canaliculi. In dead dry bone it is certain the canaliculi are tubes containing air. In *young* bone it is clear that all nutrient matter which reaches the bioplasm must permeate the matrix, and no air exists in the tubes. The organic matrix of the original tissue must remain as the diameter of the canaliculus becomes reduced by the gradual encroachment of the calcareous matter upon it, and it is possible, and indeed likely, that after a time, by the constant passage of fluid, it may be gradually dissolved away, and thus a tube, traversed by nutrient material and always containing

fluid, may result. But supposing it to remain, the portion of the matrix which occupies the canaliculi cannot be correctly termed "processes of the bone cell."

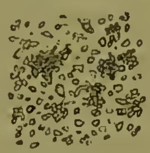
Any organic matrix remaining in the canaliculi is no doubt sufficiently permeable to transmit the nutrient fluids, but as time goes on, it no doubt loses its original firmness and by the constant action of the fluids becomes softened, and the soft tissue is in some cases at last completely dissolved away. After bone has existed for some time, the bioplasm in the lacuna dies and becomes comparatively dry. In some cases air collects in the lacunæ and canaliculi. I have seen in the bones, particularly of old persons, a very short time after death, many lacunæ and canaliculi thus filled with air, so that no doubt the air was actually in these little cavities of the bone during life. Such bone could not grow, and reparation could not have taken place had it been injured. Under no circumstances could it have passed into a state of inflammation, and had fracture occurred, union would have been impossible.

Of the ultimate structure of osseous tissue.—There has been much difference of opinion concerning the ultimate structure of bone tissue. According to some the ultimate osseous tissue is granular, while others consider that it is fibrous in character. It has been supposed that the calcareous material becomes not only thoroughly incorporated but chemically combined with the material of which the matrix of the cartilage consists. But it has been believed by other authorities that the latter is merely impregnated with the earthy salt,—that the insoluble particles are precipitated in the interstices of the tissue just as might be effected artificially in many organic substances, as, for example, thick gum or ordinary jelly. It must be admitted that arguments are not wanting in favour of both opinions upon this question.

In some instances bone may be torn in the longtitudinal direction, which lends support to the view that the tissue has been, as it were, laid down in plates or superposed laminæ, having a fibrous structure, pl. XVII, fig. 154. On the other hand, Mr. Tomes concluded from his researches that the ultimate structure of the osseous tissue was *granular*. The granules of bone are often very distinctly visible, without any artificial preparation, in the substance of the delicate spiculæ of the

cancelli, viewed with a high power, and in various sections of all forms of bone. Granules may certainly be obtained from calcined bone, either by bruising a fragment of it, or by soaking it in glycerine or syrup. They may also be made very evident by prolonged boiling in a Papin's digester. Those represented in fig. 165 were obtained in the latter mode. The granules vary in size from $\frac{1}{20000}$ to $\frac{1}{100000}$ of an inch. In shape they are oval or oblong, and often angular. In some few instances, Mr. Tomes has met with, a delicate fibrous network, which seems adapted to receive the granules in its interstices; but Mr. Tomes feels that there are some serious objections to this view. A frequent appearance of the granular-like texture of bone is represented in fig. 165.

FIG. 165.



Ultimate granules of bone, isolated and in small masses, from the Femur. (From a preparation of Mr. Tomes.) × 320.

When bone has been decalcified by immersion in acid, thin shreds corresponding to the lamellæ may be removed in a longitudinal direction. In these the minute aperture of the canaliculi which have been torn across may often be discerned. In many instances delicate transparent fibres crossing each other at different angles will be seen, showing, as Dr. Sharpey was the first to point out, that the organic matrix of bone has a fibrous structure, and is more closely allied to fibrous tissue than to cartilage in microscopical characters, as well as in chemical composition.

If bone be soaked for a long time in pure glycerine it becomes sufficiently soft to be torn without its structure being altered, as is necessarily the case when it is decalcified. Such a specimen is represented in pl. XVII, fig. 154, in which an indistinctly fibrous material has embedded in, or disseminated through, its substance a number of minute rounded particles of calcareous matter, collections of granules of Mr. Tomes. The intervals between these particles constitute the canaliculi.

A careful examination of bone at different stages of development, and under the highest magnifying powers which have been made leads us to form the following conclusions regarding its ultimate structure. The calcareous matter is at first deposited in the organic matrix in the form of minute granules which gradually increase in size and form rounded or oval particles. In the batrachia these are of considerable

dimensions. Pl. XVII, figs. 149, 150. It is not surprising that we should occasionally meet with indications of these in adult bone. Such appearances have been referred to by Dr. Sharpey, Gegenbauer, Allen Thomson, and others, but different explanations have been offered. Such globules, formed no doubt by the gradual coalescence of smaller ones, are sometimes traversed by canaliculi, and in dentine such globular masses are sometimes so arranged as to interfere, during development, with the passage of nutrient juices to the matrix which lies between them. This, consequently, remains soft and uncalcified, and when the tooth is dried, spaces result between the several globules. These spaces, of course, then contain air, and appear black when the dentine is examined by transmitted light. Dr. Sharpey states that he has found layers of rounded nodules, near the surface of the shaft of long bones, lying among the circumferential laminæ, and accepts the explanation of C. Loven, of Stockholm, who thinks that these botryoidal masses correspond to depressions made in a corresponding portion of bone by the process of excavation. In a cross section of a large serpent's rib, Dr. Sharpey noticed an outer and inner series of concentric lamellæ, which could be easily peeled from one another after decalcification. The detached surfaces showed elevations and corresponding depressions. Many of the former contained one, two, or three lacunæ in their substance.

Whenever earthy salts are deposited in an organic matrix they tend to form these nodular aggregations and botryoidal masses, as was first shown by Mr. Rainey, who caused calcareous salts to be deposited in gum, gelatine, and other transparent organic matters of the same kind. Whether bone tissue should be regarded as an organic matrix merely infiltrated with the earthy salts,—a mere admixture of the organic and earthy matter, or a true chemical combination of earthy and animal matters, is a question which still remains open to discussion.

Of the Vessels of Bone.—We now proceed to inquire into the manner in which the distribution of blood to bone is provided for. A texture undergoing constant change, containing much animal matter, and needing a constant supply of inorganic material, must necessarily be largely supplied with blood, the common source of the nutrient materials of all tissues.

The blood-vessels of bone are very numerous, as may be satisfactorily seen on examining a well-injected specimen. The arteries of the compact tissue are in great part derived from those of the periosteum, and pass into the canals obliquely. If the periosteum be torn from the bone, these vessels can always be seen without difficulty. The vessels which penetrate the cancellated texture of the extremities of the long bones are very large, and their branches ramify freely among the cancelli.

The vessels of the membrane of the medulla which is contained in the shaft, receive their blood from a special artery that pierces the compact tissue through a distinct canal, known as that for the nutritious artery. This vessel immediately divides on entering the medullary canal; of the branches, one ascends, the other descends, and both break up into a capillary network, anastomising with the plexuses in the extremities of the bone, derived from the arteries that penetrate there. From the copious vascular network thus formed within the bone, the innermost part of the compact substance of the shaft receives its blood-vessels.

Haversian systems, and rods.—The arrangement of the vascular canals was discovered by Clopton Havers, who showed that these channels were pretty uniformly distributed through the compact tissue, and inosculated everywhere with one another. In the long and short bones they follow the same general direction as the axis of the bone, and are joined at intervals by cross branches. The meshes thus formed are more or less oblong (fig. 166). The deeper ones open into the contiguous cancelli, with the cavities of which they are continuous.

Fig. 166.

Haversian canals, seen on a longitudinal section of the compact tissue of the shaft of one of the long bones:—*a*. Arterial canal. *b*. Venous canal. *c*. Dilatation of another venous canal.

The arteries and veins of bone usually occupy distinct Haversian canals. Of these the venous are the larger, and commonly present at irregular intervals, and especially where two or more branches meet, are pouch-like dilatations (*c*, fig. 166), calculated to serve as reservoirs for the blood, and to delay its

outward flow. In many of the large bones, particularly in the flat and irregular ones, the veins are exceedingly capacious, and occupy a series of tortuous canals of remarkable size and very characteristic appearance. These are well described by Breschet in his elaborate work on the venous system; from which the accompanying figure (fig. 167) is taken. The canals run, for the most part, in the cancellated structure of the bones, and are lined by a more or less complete layer of compact tissue, which itself often contains minute Haversian canals. The veins they contain discharge themselves separately on the surface.

Fig. 167.

Venous canals in the diploë of the cranium.—After Breschet.

The Haversian canals vary in diameter from $\frac{1}{2500}$ to the $\frac{1}{200}$ of an inch, or more, the average being about $\frac{1}{500}$. Their ordinary distance from one another is about $\frac{1}{120}$ of an inch. They may be regarded as involutions of the surface of the bone, for the purpose of allowing vessels to ramify in its substance in great abundance. It is evident that the cancelli, and even the great medullary canal itself, are likewise involutions of the osseous surface, though for a partly different end. These larger and more irregular cavities in bone may be considered as a dilated form of Haversian canal. They contain vessels not only for the nutrition of the thin osseous material forming their walls, but also for the supply of the fat enclosed within them.

Thus the true osseous substance may be described as lying in the interstices of a vascular membrane, or of a network of blood vessels. The most interesting points in the minute anatomy of bone relate to the mode in which nutrition is provided for in those parts not in immediate contact with the blood-vessels. We have already seen that considerable masses of cartilage derive their nutriment from vessels placed on their exterior only, apparently by a kind of imbibition; but bone, which is of a far harder and denser nature, is unable to imbibe

its nourishment so easily. Hence its surface is greatly augmented by the arrangements already detailed; and, in addition to this, as has been already shown, the osseous tissue itself is provided with a special system of microscopic cavities, "*lacunæ*," and "*canaliculi*," or pores, by which its recesses may be irrigated, to a degree greatly exceeding what could have been effected by blood-vessels alone, consistently with the compactness and density required in the tissue.

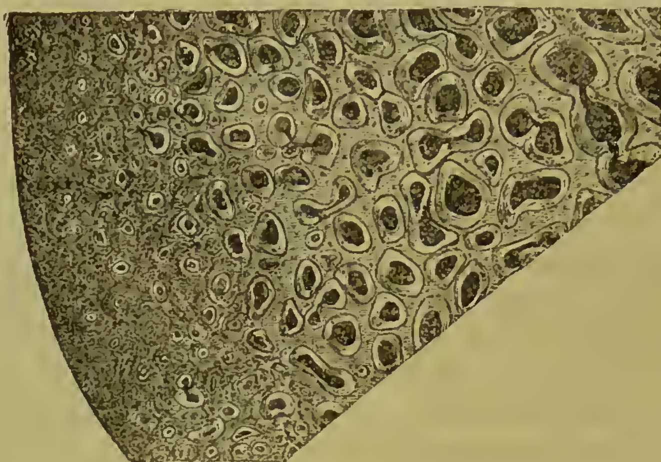
The bony tissue with its canaliculi and germinal matter always has a certain definite relation to the vessels. It may exist as a simple thin lamina, covered upon each side with a highly vascular membrane, or as solid cylindrical processes often arranged so as to form a network, also invested with a vascular membrane; or the osseous tissue may be arranged in concentric laminæ round the central vascular canal of Havers, which in the living bone is occupied by a minute vessel, around which are numerous small living particles, masses of germinal matter or bioplasm. These living bioplasts are concerned in the growth and removal of the osseous tissue. *See* p. 278.

Of a thin plate of bone the tissue in the central part is the oldest. Of a solid cylinder, that in the centre was first formed, while of the laminæ of the Haversian system, those at the *circumference* are the oldest, and the laminæ close to the central vessel were the last developed. The first two forms of bony tissue constitute the cancellated structure, and the last (Haversian systems) make up the compact tissue of bone; but, as would be supposed, transitional forms exist, and if the thin laminæ of bone forming the boundaries of spaces be very much thickened by the formation of new laminæ within them, the arrangement of the Haversian system is approached; while, on the other hand, if the canal in the centre of several adjacent Haversian systems be very much increased in size, in consequence of the multiplication of the bioplasts and the removal of the bone tissue, we should get an arrangement very like that seen in the cancellated texture. These differences are not fanciful, but such transitions can actually be demonstrated in almost all bones.

A section of a growing stag's antler affords a very beautiful example of Haversian systems, and shows how the bony tissue grows around the blood-vessels (fig. 168). In the central part are

seen enormous vessels separated by very thin layers of bony tissue. As we pass towards the circumference the diameter of

FIG. 168.



Section of the antler of the stag near the tip of one of the cusps. The centre is marked *a*. At the outer part, *b*, the formation of Haversian systems is nearly complete, but towards the centre enormous Haversian canals are occupied by air-vessels, black in the drawing. From a specimen prepared by Mr. White. × 20.

the vessel becomes less, just as the ring of bone is seen to be increased in thickness, until near the surface of the antler the central cavity or Haversian canal is reduced to a mere line. The vessel has wasted, and the blood has ceased to flow. Similar changes gradually proceed in every part of the antler, which at length becomes a mass of bloodless and perfectly dead osseous tissue. This being cast off, is replaced by a new antler which passes through all its stages of development like the one that preceded it. In ordinary perennial bone the vessel in the Haversian canal often becomes very small, but it is very seldom that it ceases to transmit blood or completely wastes. A portion of fig. 168, representing four Haversian rods near the circumference of the antler is seen in fig. 169.

FIG. 169.

Haversian systems fully formed from the outer part of Fig. 168, but magnified 215 diameters, showing lacunæ and canaliculi.

A longitudinal section of the antler will give the student a very correct notion concerning the arrangement of the

Haversian vessels, and the manner in which they are connected together by transverse branches, figs. 169 and 170. The draw-

Fig. 170.

Longitudinal section from the same specimen as fig. 168, showing the communications between the very large vessels in the Haversian canals. × 20.

ings have been copied from beautiful preparations which were made by our friend Mr. T. Charters White.

The reader will now readily comprehend the apparently complex arrangement of the compact osseous tissue. Let us take for example one of the long bones. The entire vascular surface consists of—1, the *outer surface*, covered by the periosteum; 2, the *inner surface*, lined by the membrane of the medullary cavity and of the cancelli; 3, the *Haversian surface*, or that forming the canals of the compact tissue, and having in contact with it the vascular network that occupies them, and which has been already described. These involutions of the surface are so arranged that no part of the osseous tissue is in general at a greater distance than $\frac{1}{170}$ of an inch from the vessels that ramify upon them.

There is a layer of tissue upon the exterior of the bone deriving its nourishment from the periosteum, and which may be called the *periosteal layer*. The periosteal pores of the superficial lacunæ of this layer open upon the surface. There is another layer, forming the immediate wall of the medullary cavity, and termed the *medullary layer*. Its lacunæ, in like manner, face this cavity; and the pores of the inner ones open upon it. This layer may be said to be folded so as to invest the plates and fibres of the cancelli; and all the lacunæ of these

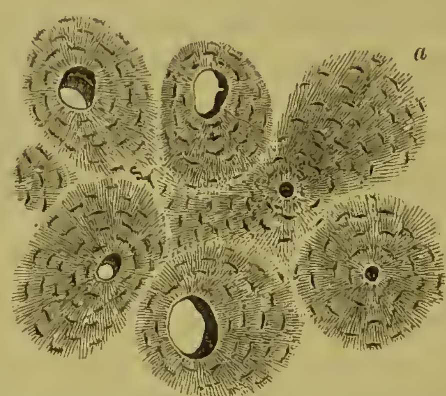
face these irregular cavities, and their pores open into them. The Haversian surface, too, being an involution of the outer and inner surfaces, and serving to connect them has been said to be formed by an involution of the periosteal and medullary layers, and to unite these with one another. Where a vessel enters the compact tissue from the exterior, it carries with it a sheath of bone from the periosteal layer. The lacunæ of this osseous sheath, instead of being turned outwards, like those of the periosteal layer, preserve their relation to the vascular surface to which they pertain, and face *inwards* towards the vessel. Wherever the vessel penetrates, whatever direction it takes, and however it branches, it is everywhere accompanied by this sheath from the periosteal layer, or by offsets from it; and, when it enters the medullary canal, its sheath expands into the medullary layer.

As the vessels of the compact tissue take a longtitudinal direction, a transverse section of the bone (fig. 171) will appear pierced by numerous holes, which are the Haversian canals cut across. Each hole appears as the centre of a roundish area, which is the section of an involuted periosteal layer now become

FIG. 171.

Transverse section of the compact tissue of a long bone; shewing, *a*, The periosteal layer; *b*, The medullary layer, and the intermediate Haversian systems of lamellæ, each perforated by an H. canal.—Magnified about 15 diameters.

FIG. 172.



Part of the preparation represented in the last figure, more highly magnified; shewing the package of the Haversian systems, and also the light spaces between neighbouring ones, The system, *a*, appears to fill up an interval between the others. The lacunæ are seen facing the Haversian canals, and the pores taking a general radiating direction. At *s*, an irregular lacuna.

a vertical rod, containing a vessel in its axis. The Haversian canals vary considerably in size, and do not maintain a very close relation to the thickness of their respective osseous walls.

They are frequently eccentric, owing to their wall bulging more in one direction than another, to fit in between others in the vicinity; for though the rods of bone, containing the vessels, affect the cylindrical form, they often present an oval, or even a very irregular figure, on a section; their close package having modified their form.* The periosteal and medullary layers are also well seen on the same section, the latter curving inwards to constitute the walls of the cancelli. These two layers are of very irregular thickness.

The *lamellated* character of bone can be distinguished in the periosteal, medullary, and Haversian layers; and, in general, wherever several successive series of lacunæ exist. The Haversian rods, however, are remarkably prone to exhibit this appearance. Their lamellæ, however, are not concentric, as commonly described. The fissures which disclose them are indeed concentric, but they are always incomplete, never extending completely round the canal; so that the lamellæ run into one another at various points. This results from the fact that the lacunæ are not arranged in sets equidistant from the centre, but are scattered, as it were, independently of one another, at every possible variety of distance from the canal (fig. 146, p. 245 and 172). The larger concentric cracks, which generally run through the lacunæ, seem to occur where two or three of these happen to lie nearly in the same curve. Bone is very apt to crack in the interval between the rods; and each of these rods is really so distinct from those near it, that it may be designated conveniently, for the purposes of description, as an *Haversian system of lamellæ.*

Fig. 173.

Transverse section of the compact tissue of a tibia from an aged subject, treated with acid; showing the appearance of lamellæ surrounding the Haversian canals. Portions of several systems of lamellæ are seen. The appearance of the lacunæ, when their pores are filled with fluid, is also seen, as well as the radiation from the canals which then remain.—From Mr. Tomes.

* The irregular size and outline of the Haversian canals thus noticed by Todd and Bowman have been fully explained by the researches of Tomes and De Morgan. See page 267.

In a longtitudinal section of the compact tissue of a long bone the appearance of lamellation (fig. 173) is generally less evident, except where a longtitudinal canal happens to lie exactly in the plane of section. This lamellated arrangement appears to be due to the circumstance that the osseous tissue is formed in successive layers, a process which was first satisfactorily described by Messrs. Tomes and De Morgan in their memoir already referred to (Phil. Trans, 1853).

The description now given of the intimate texture of the compact tissue of long and short bones will apply, in all essential respects, to every other example of the compact tissue; the chief difference consisting in the direction taken by the Haversian canals, which is irregular where the tissue follows an irregular course. In general, however, the canals, with the Haversian rods forming their sheaths, run in the direction in which the tissue needs the greatest strength. Thus, in the long bones it is vertical; and in those flat bones, which have to support weight, it is also more or less vertical; while in those designed to sustain the action of forces of other kinds it is liable to corresponding variety.

So beautifully mechanical is this disposition of the Haversian systems in the compact tissue, that we need not smile at the descriptions of Gagliardi, who, with imperfect means of observation, appears to have been at least faithful in his attempts to delineate nature. The periosteal and medullary layers are true *plates* of bone, and the Haversian systems are true fibres or *pins*, all connected with one another by direct continuity of tissue, and most artfully arranged for the mechanical ends in view; and we cannot sufficiently admire the skill which has caused the means, employed for these ends, to conspire with those which were indispensable for the due nutrition of the tissue.

In the ordinary cancellated texture, each cancellus must be regarded as a little medullary cavity, containing, as it does, medulla and highly vascular medullary membrane. The plates of bone which form its walls consist of lamellæ, among which lacunæ, with their pores, are scattered; and they sometimes, when thick, contain Haversian canals. Usually, however, the pores of these laminæ communicate directly with the cavity of the cancellus to which they belong.

Haversian Spaces.—Not only does the compact tissue of bone gradually pass into cancellated structure, as described on p. 261, but comparatively large spaces, like cancelli, are to be demonstrated in the compact tissue of a long bone. These are the *Haversian spaces* of Messrs. Tomes and De Morgan, who have proved most conclusively that, during the life of the bone, the *canals* become larger, and are converted into *spaces* by erosion, the removal of the bone tissue taking place in a direction from within outwards. In adjacent spaces the opposite processes may be going on at the same time. The *formation* of bone takes place from without inwards. An *Haversian space* therefore gradually contracts to form a *canal*. The Haversian canals and spaces are seen in a section of dry bone as openings, but in the recent bone they are occupied by a vessel which is surrounded by soft pulpy matter, consisting of a little connective tissue near the vessel, but composed mainly of small living bioplasts. These bodies are also found on the deep layer of the periosteum and medullary membrane, as has been described. They exist in considerable number wherever bone is being formed, and are, in fact, the active agents concerned in the removal of the old bone tissue, and in the formation of the new osseous lamellæ.

Now, the process of erosion or removal of an Haversian system does not take place quite regularly, for part of an Haversian system may be left while neighbouring systems may be entirely removed. When the formation of the new Haversian system commences in the space scooped out, it is obvious that *new* laminæ will be deposited over those which originally belonged to the *old system*. This is why "interstitial laminæ" are always seen between the Haversian systems in a section of the compact tissue of bone, and we are indebted to Messrs. Tomes and De Morgan for their very clear and satisfactory explanation of this most important fact.

When bone is removed by absorption, as in the excavation of Haversian spaces, the surface is sometimes irregularly excavated, so as to give rise to a number of small pits or depressions which, after a time, are filled up by the deposition of new bone. If this latter be removed it will be found to form as it were a *cast*, and appears nodulated or covered with botryoidal masses of bone tissue. This fact has been referred to by

Sharpey, who accepts the above explanation, which was first suggested by Loven, of Stockholm. (Quain's Anatomy, seventh edition, 1866. "General Anatomy," by Dr. Sharpey, page xcviii.)

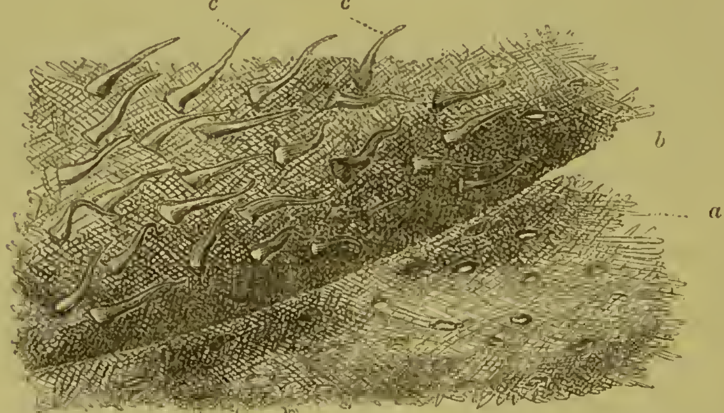
Perforating Fibres of Bone.—Dr. Sharpey has discovered some very peculiar fibres which perforate the lamellæ, and as it were pin them together. These have been termed by him

FIG. 174.

Magnified view of a perpendicular section through the external table of a human parietal bone, decalcified. At *a*, perforating fibres in their natural situation; at *b*, others drawn out by separation of the lamellæ; at *c*, the holes or sockets out of which they have been drawn. (H. Müller, Quain's Anatomy, 7th ed.)

perforating fibres. The holes through which they pass are often seen in detached laminæ. They are most easily demonstrated

FIG. 175.



Lamellæ torn off from a decalcified human parietal bone at some depth from the surface; *a a*, lamellæ, showing reticular fibres; *b b*, darker part, where several lamellæ are superposed; *c c*, perforating fibres. Apertures, through which perforating fibres had passed, are seen, especially in the lower part of the figure. Magnified about 200 diameters, but not drawn to scale. (Altered from a drawing by Dr. Allen Thomson, in the 7th edition of Quain's Anatomy.)

in the parietal bone, but are to be found in other situations. They have been observed by Kölliker to exist in great numbers in fishes and Amphibia, and Sharpey has no doubt of their existence throughout vertebrata. H. Müller, of Wurzburg, has stated that some of these fibres are of the nature of yellow elastie tissue, and he explains the tubes which are oeeasionally met with in bone, and were deseribed by Tomes and De Morgan, by supposing that the uncalcified perforating fibres which originally occupied them had become dried up. Sharpey eoncurs in this explanation. It is not inprobable that some appearances occasionally seen in the perpendieular seetions through the eompact tissue of the flat bones of the eranium may be due to a modification of the ossifying process oeeurring in the remains of the vessels and connective tissue which existed at an early period of embryonic life, and formed a temporary tissue, in which the development of true bone was subsequently earried out.

Periosteum and Medullary Membrane.—The periosteum is usually described as a fibrous membrane, whieh gives support to numerous nerves and blood-vessels. Its outer layers exhibit a simply fibrous strueture, but its deeper portion, whieh is eontinuous with the bone tissue, exhibits a totally different anatomieal arrangement. Here are seen a number of elementary parts of unossified bone tissue, each eonsisting of an oval mass of bioplasm invested by a soft formed material. The deeper layer of the periosteum of a young animal is the seat of the formation not only of new bone but of eomplete Haversian systems. The elementary parts multiply and the eapillary vessels are gradually enclosed by the growth of tissue, whieh at length undergoes ossifieation, see fig. 187, p. 282. This proeess has been fully described by Messrs. Tomes and De Morgan.

The vessels from both periosteum and medullary membrane pass into the openings of Haversian eanals, and when these membranes are gently torn away from recent bone, the small vessels may be seen without diffieulty, extending from the deep surfaee, and penetrating into the canals of the eompaet tissue.

It has been shown by M. Ollier, of Lyons,* that if portions of the periosteum be transplanted to various parts of the organism,

* "Journal de la Physiologie," tom. ii., pp. 1 and 169.

bony tissue will be formed in the new situation. This process is due to the growth and development of the masses of bioplasm which exist in such great number at the deep surface of the fibrous periosteum. These grow and multiply, and produce formed material, just as if they had remained in the original seat of their development—a striking proof that the *kind* of tissue formed by living matter depends upon its *powers* rather than upon its position or the conditions to which it is exposed. In certain forms of bone cancer very minute portions of actively growing bioplasm are sometimes carried to the lungs, and grow and multiply and give rise to bone cancer in the pulmonary tissue, proving that the bioplasm possesses the peculiar property or power of forming this particular tissue if supplied with pabulum.

Of the medulla or marrow of bone.—The medulla of bone is a form of almost pure adipose tissue, which contains very little areolar tissue associated with it. It is a question of great interest how this adipose tissue is produced. It fills the cancelli, and exists in quantity in the medullary cavity, and is even found in large Haversian canals. There is no doubt that the elementary parts which form at length the fat cells of the marrow, are the direct descendants of the bioplasts which gave origin to the cells converted into bone. The proper marrow cells (myeloid cells) may become converted into bone-tissue or into marrow. During development, as would be supposed, these "myeloid" cells contain little or no fat, but as the bone attains its permanent character, many of the cells become "fat cells" instead of being converted into bone-tissue. In the majority of birds these cells do not form fat, but as the bones are freely penetrated by air, the matter which would be fat under other circumstances, is probably oxidised as fast as it is produced, and caused to be eliminated as carbonic acid.

Of Myeloid Cells and of the formation of the plates and spiculæ of the Cancellated Tissue.—The little plates or cylindrical spicules of bone which enter into the formation of the cancelli are represented at first by soft masses, consisting of several elementary parts of bone. These masses may often be detached, when they are found to have the appearance of large compound cells, consisting of many smaller ones. They are met with in numbers beneath the periosteum as well as in the medullary

cavity, and in disease the soft spongy tissue which is formed in connexion with the bone consists of soft masses of this kind. These are the so-called *myeloid cells*, which are really composed of the bioplasts of bone. At an early period of development, the myeloid cell consists only of several small oval masses of germinal matter, the outer part of each of which is undergoing conversion into soft formed material. This compound mass gradually increases, and at a subsequent period becomes impregnated with calcareous matter, and thus a thin plate, or a cylindrical column or a delicate thread of bone-tissue is formed.

In fig. 185, pl. XIX, p. 278, a good specimen of the so-called myeloid cells from one of the cancelli of the bone of the great toe is represented. Two or three of the masses are elongated and much bent. These might become ossified and converted into the spicules of bone which form the imperfect septa between the cancelli. Around these are many small granular cells, and it is interesting to notice the fact, that while the first structures have a dark-red colour in the specimen, the latter are scarcely tinged with the carmine, although both have been exposed to the influence of the fluid in the same way. The first was growing actively, the last was comparatively inactive, and there can be no doubt that it was being gradually removed as the former structure advanced in development. What remained would then become the medulla, and many of the "cells" would eventually assume the character of "fat cells."

Nerves of bone.—In the periosteal membrane of the frog fine pale nerve fibres may be detected ramifying here and there in the tissue itself, in addition to those which are distributed to the vessels. A similar arrangement is seen in the *dura mater*, and in the *sclerotic coat of the eye*, and in tendinous expansions composed of white fibrous tissue.

Nerve fibres are distributed to the vessels of bone, as well as to the vessels of other tissues, but it is doubtful if the bone tissue itself is supplied with nerve fibres. It is true that bone like many other textures which in a state of health are almost insensitive, becomes, when inflamed, intensely sensitive, but this fact may be explained, as in other cases, by changes which have affected the nerves which are distributed to the capillary vessels in great number. [L.S.B.]

THE DEVELOPMENT OF BONE.

In the earliest period of life at which the skeleton can be detected amongst the soft pulpy tissue of which the embryo is constituted, it is found to consist of "cells" or elementary parts forming the simplest form of cartilage. The formed material which at first is so soft as to be destroyed by very slight pressure of the finger, gradually acquires consistency, loses water, and slowly increases in density and firmness. The temporary cartilages of the mammalian skeleton have the same general shape before as after their ossification; and as this process is slow, and not finally completed until adult age, they share during a considerable period in the functions of the bony skeleton.

In *mammalia*, bone commences to form at a very early period of intrauterine life in two ways: 1. *By the ossification of temporary cartilage.* 2. *By the ossification of fibrous membrane.*

The temporary cartilage exhibits the same shape as the future bone is to assume, but it contains no medullary cavity. It gradually undergoes conversion into a temporary and imperfect kind of osseous tissue, which is afterwards removed, and true bone formed in its stead.

The formation of the *permanent bone* in mammalia corresponds in all essential and important particulars with the process which occurs in fibrous membrane (*see* page 280), and which results in the formation of osseous tissue. This fibrous texture is not preceded by any form of cartilage.

Now, in the frog, the changes which occur during ossification accord with those which have been described as taking place in the temporary cartilage of the bones of the skeleton of man and mammalia; but the changes proceed gradually until the bone is complete, instead of ceasing at a very early period, before, in fact, true bone is formed, as occurs in the latter. In many of the lower vertebrata, which continue to grow as long as they live, the bones gradually increase in extent during a considerable period of life, and the formation of the perfect bone results from gradual and uninterrupted changes occurring in the cartilage, new cartilage tissue being produced beyond the bone already completely developed.

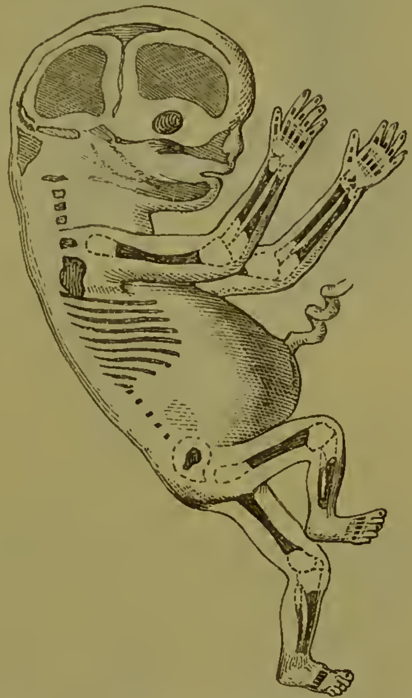
In man the temporary cartilages increase in bulk by an interstitial development of new cells until the full growth is attained. A few vessels, also, shoot into them at an early period, occupying small tortuous canals, which subsequently become obliterated.

Ossification commences in the interior of the temporary cartilage at determinate points, hence called *points* or *centres of*

Fig. 176.

Human fœtus, about the eighth or ninth week of intrauterine life, soaked in alcohol and soda, and preserved in glycerine. *a*, heart; *b*, stomach; *c*, intestine, not yet much longer than the body. The branch below the letter is the remains of the omphalo-mesenteric duct. *d*, lungs; *e*, supra-renal capsules; *f*, kidneys; *g*, remains of Wolffian bodies, with ovaries and genital ducts. Points of ossification are observed in the humerus, radius, ulna, last phalanges of the fingers, femur, tibia, and ribs. The ossification of the clavicle is advanced, but no ossific points are yet to be detected in the feet. Natural size.

Fig. 177.



Human fœtus, about the eleventh or twelfth week. Ossific points are observed of considerable size. But one point exists in the os innominatum and two are seen in the scapula. The shading in the head and face indicates the formation of bone. The ossification of the first and third phalanges of the fingers and metacarpal bones has advanced, but at present there is only one point of ossific deposit in the tip of the great toe and one for the middle toe. In both drawings the development of the anterior extremities is much more advanced than that of the legs. Soaked in soda and alcohol for a few days, and preserved in spirit. Not changed since 1853–4. Natural size.

ossification. From these the process advances into the surrounding substance. The period at which these ossific points appear varies much in the different bones, and in different parts of the same bone. The first is the clavicle, in which the primitive point appears during the fourth week: next is the lower jaw; the ribs, too, appear very early, and are completed early; next, the femur, humerus, tibia, and upper jaw. The vertebræ and pelvic

bones are late, as well as those of the tarsus. See figs. 176, 177. Some bones do not begin to ossify till after birth, as the patella.

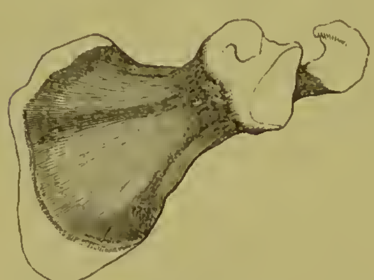
It is not possible to demonstrate by the ordinary process of dissection, or by maceration, the points of ossification which are first formed at a very early period of development of the embryo, but if the soft tissues be made transparent, every spot of earthy matter in the skeleton may be observed most distinctly as soon as it appears, and by condensing a strong light upon the various parts of the skeleton properly prepared, the youngest ossific points are beautifully seen. Figs. 176 and 177, which represent fœtuses at the eighth or ninth week, and at the end of the third month, respectively, have been copied from specimens prepared by soaking some time in an alkaline fluid.*

Fig. 178.

Vertical section of the knee-joint of an infant; showing the points of ossification in the shaft and epiphysis of the femur and tibia, and in the patella. A few vascular canals are also seen in the cartilage. Natural size.—From the Museum of King's College.

In many bones the ossification of the temporary cartilage begins at more than one point. Thus, in the long bones, fig. 178, there is a middle point, to form the future shaft; and one at each extremity, to form the articular surface and eminences. That in the shaft is the first to appear, and the others succeed it at a variable interval. The central part is termed the *diaphysis,* and for a long period after birth there remains a layer of unossified cartilage between this and the *epiphyses,* as the extremities are then styled. *Processes* of bone have usually their

Fig. 179.

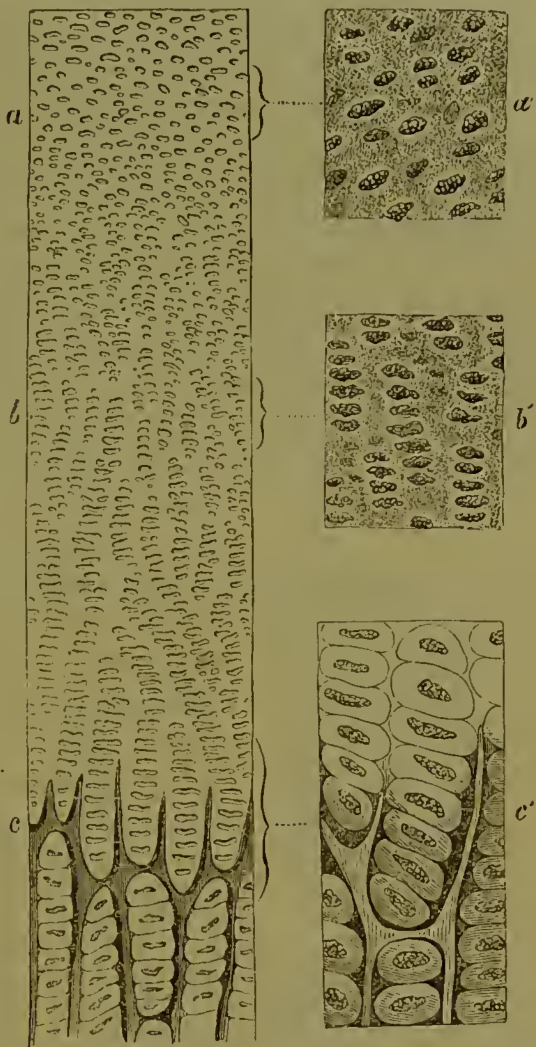


Scapula of a fœtus at the seventh month; shewing the progress of ossification. Natural size. The light parts are epiphyses as yet cartilaginous.—From the Museum of King's College, London.

* I have obtained excellent results from the use of a fluid composed of alcohol

own centres of ossification, and are termed *epiphyses* until they are finally joined to the main part, after which they receive the name of *apophyses*.

Fig. 180.



Vertical section of cartilage near the surface of ossification;—*a*, Ordinary appearance of the temporary cartilage. *a'*, Portion of the same more highly magnified. *b*, The cells beginning to assume the linear direction. *b'*, Portion more magnified. Opposite *c*, the ossification is extending in the intercellular spaces, and the rows of cells are seen resting in the cavities so formed; the nuclei being more separated than above. *c'*, Portion of the same more highly magnified.—From a new-born rabbit which had been preserved in spirit.

Ossification generally extends in the direction that the future laminæ and Haversian rods are to assume, and which corresponds in a great measure to that in which it is designed that the chief strength of the structure may lie. Thus, in the bones composing the vault of the cranium, there is always a very decided radiation from the most prominent part of the convexity of each, fig. 177. In the scapula this direction is indicated by the lines of shading in the accompanying fig. 179. The outline marks the limits of the temporary cartilage at the time, but these would have extended had the bone been left to grow.

Of the early changes occurring during the ossification of Temporary Cartilage.—The temporary cartilage of the fœtus undergoes very important changes prior to the deposition of the calcareous matter

and solution of caustic soda, in the proportion of eight or ten drops to each ounce of alcohol. Many tissues are, at the same time, rendered very hard and transparent in such a mixture. It is especially useful in tracing the stages of ossification in the early embryo. It renders all the soft tissues perfectly transparent, but exerts no

in the matrix. In the vicinity of the point of ossification, for example, in one of the long bones, the "cells" are seen to become gradually arranged in linear series, which run down as it were towards the ossifying surface. The appearance they present on a vertical section is represented in fig. 180. At first their aggregation is irregular, and the series small (*b b′*); but, nearer to the surface of ossification, they form rows of twenty or thirty. These rows are slightly undulated, and are separated from one another by the matrix or intercellular substance.

The masses of germinal matter or bioplasm of temporary cartilage are small, and pretty uniformly scattered through a sparing homogeneous matrix, but as they become arranged in rows they increase in size, *c′*, are closely applied to one another, and are compressed. This is observed near the ossifying surface, and it is probable that as change advances in this situation, the matrix becomes more permeable to nutrient matter, and hence the bioplasts increase in size. The nuclei or new centres of growth are often large and very distinct, especially in the elementary parts which have become embedded in the temporary bone.

FIG. 181.

Horizontal section of the ossifying surface of a fœtal bone; shewing the cups of bone cut across, with the granular nuclei of the included "cells." *a*, New bone. *b*, Nucleus.—From the rabbit. Taken from a drawing of Mr. Tomes.

The lowest row of bioplasts appears to dip into, and rest in the deep narrow cups of bone, formed by the osseous transformation of the "intercellular substance," between the rows. These cups are seen in a vertical section in fig. 180, *c c′*, and in a transverse section on the level of the ossifying surface in fig. 181. As ossification advances between the rows, these cups are of course converted into closed areolæ of bone, the walls of which are lamelliform, and at first extremely thin.

action on the earthy matter of the developing bone. The most minute ossific points can therefore be very readily discovered. A fœtus, prepared by being soaked for a few days in this fluid, and preserved in weak spirit, forms a very beautiful preparation. The specimen figured was prepared eighteen years ago (1853–4), and still preserves its transparency. The practical advantages of such a plan over the usual very laborious process of dissection, in investigating the periods of ossification in various bones, are obvious. This fluid will also be found very useful in studying the structure of many soft granular organs. I found it of special service in investigating the anatomy of the liver. [L.S.B.]

The calcareous matter is mainly deposited in the formed material between the lines of cells, so that a network of temporary and brittle spongy bone tissue is formed. In these crypts or spaces the cartilage cells remain, and their 'nuclei' still retain their vitality. Calcareous particles are also deposited in the material of which the outer portion of the elementary part consists, and which has been termed the "cell-wall."

The vessels advance close to the seat of these changes, and it is possible that the passage of the nutrient pabulum from the vessels, for the most part in linear streams parallel to the long axis of the bone, as from a base, may determine the linear arrangement and the enlargement of the cells already spoken of. Moreover, as the calcareous matter must have been carried in a state of solution to the matrix, where it is precipitated, it is obvious that at the point where the cells are the largest, much fluid has been set free, and it is probable that this may in part be taken up by these cells.

Temporary cartilage contains many vascular canals, and the *youngest* cartilage cells are situated nearest to these. The rate of growth of the cartilage cells and the formation of matrix gradually diminishes as we pass from the canals. The vascularity of the *bone* is, however, far greater than that of the cartilage, and thus the greater supply of pabulum and the more rapid change at the ossifying surface are explained.

The production and removal of Temporary Bone.—The changes which have been already described result in the formation of a soft spongy network of very brittle temporary bone, pl. XIX, fig. 182, at *a*. Such a tissue, though useful for a short time, when strength was not a requirement, would be quite unserviceable for supporting the weight of the body, or for the attachment of muscles to move the limbs. This temporary bone is so fragile that it may be easily crushed between the finger and thumb. It consists merely of the soft matrix of the temporary cartilage irregularly infiltrated with calcareous matter, which has been very quickly precipitated. No sooner is this brittle tissue formed than changes begin to take place in it.

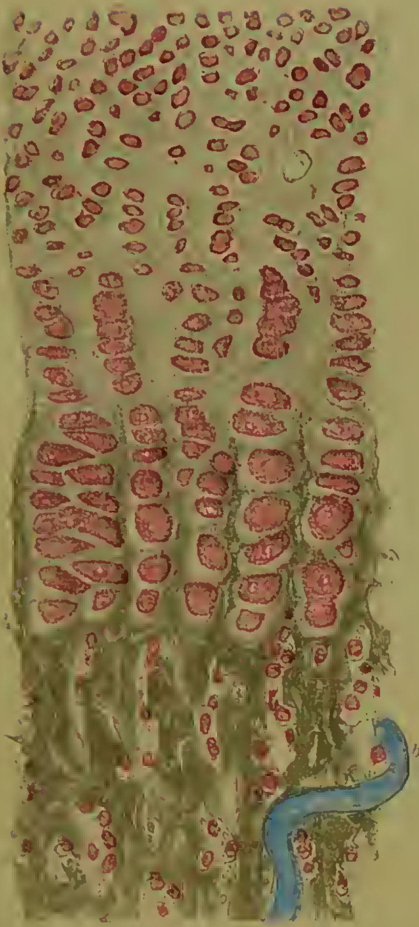
If we examine the shaft of a long bone in which ossification has just commenced in the central part, as represented in fig. 177, we shall find that calcareous matter is deposited throughout the entire thickness. The temporary cartilage,

which the shaft of the bone was first constituted, was solid. There is no cavity in the cartilage corresponding to the medullary cavity in the permanent bone. The temporary ossification therefore affects the whole thickness of the shaft. In the subsequent changes, not only is temporary bone removed, but that which occupied the central part of the shaft is never replaced by bone at all. A permanent space is found which in most of the bones of birds is filled with air, but in those of other vertebrata is occupied with a form of adipose tissue, the *marrow*, *myelon*, of the bone. As the bone grows in circumference it is clear that all the spongy bone first formed must be removed by absorption, for the medullary cavity with its marrow occupies the very spot where the temporary cartilage was first developed.

The formation of Haversian systems and the exact position of the vessels is determined by the changes proceeding beneath the periosteum, which are figured in pl. XIX, figs. 183, 184, and in fig. 187, and which are described on page 282. The germinal matter or bioplasm of the original cartilage is instrumental in effecting this change. The spaces or crypts of the soft brittle temporary bone were of course occupied by many of the cartilage bioplasts, pl. XIX, fig. 182. Soon after the spongy bone is produced, these, or at any rate many of the bioplasts situated in the central part, where the process of calcification commenced, increase in size and number, while at the same time the spicules of temporary bone are eroded and become reduced in thickness. They get soft, and in places actually undergo disintegration into granules. The originally smooth surfaces are now rough, and scooped out into little pits in consequence of the eroding action of the living growing bioplasts. These in fact live and grow at the expense of the spongy temporary bone, and at last a cavity is formed, which is occupied by multitudes of bioplasts, the descendants of those of the temporary cartilage; bounding this is a thin shell of temporary bone, which has been formed beneath the periosteum, and lastly, and most externally, is this membrane itself.

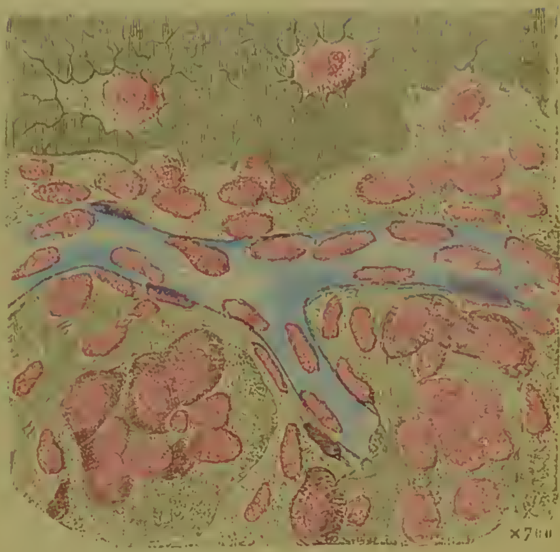
We see then what becomes of the so-called nuclei of the original cartilage cells after the formation of the temporary bone in the fœtal cartilage. That they remain active while the disintegration of the temporary bone is proceeding, has

Fig. 1[illegible]



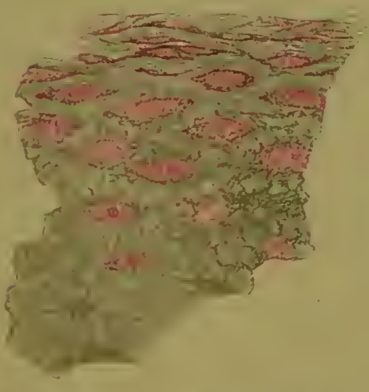
[illegible] formation of temporary [illegible] (a) [illegible] of the human fœtus [illegible] crypts or spaces [illegible] the [illegible] are seen numerous [illegible]plasts [illegible] descendants of the [illegible]plasm [illegible] b A capillary [illegible] × 130. p. 278, 28[illegible]

Fig. 18[illegible]



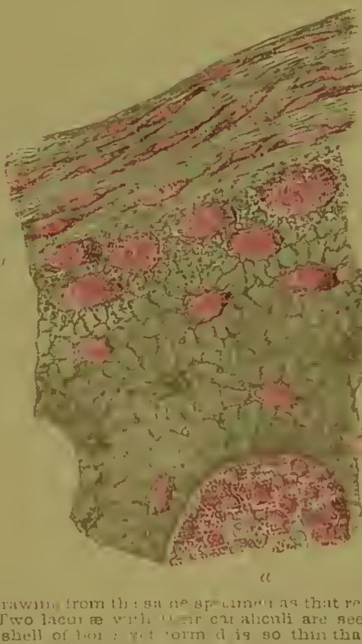
Portion of cancellated structure with contents of the "cancelli" from the first phalanx of the great toe of a girl about 16 years of age. a, portion of the fully formed osseous tissue. About the central part of the figure is a spot where it would appear that the bone is being gradually removed. On a line with b are several bioplasts with matrix which has not yet undergone calcification. c, a capillary vessel with bioplasts. d, the soft material round the bioplasts has a slightly fibrous character. e and f collections of bioplasts from which the bony plates and spicules of the cancelli are formed. These are the so-called "myeloid cells." × 700. p. 271.

Fig. 183.



[illegible] beneath the periosteum [illegible] from [illegible] at the [illegible]th month [illegible] permanent [illegible] of the [illegible] are seen [illegible] filled with air. × 300. p. 2[illegible]2.

Fig. 184.



Another drawing from the same specimen as that represented in Fig. 183. Two lacunæ with their canaliculi are seen to contain air. The shell of bone yet formed is so thin that portions of cancelli are included in the specimen and one cancellus, a, is entirely occupied with bioplasts. The permanent bone increases by the formation of new bone tissue immediately beneath the periosteum, at a a. × 300. p. 282.

$\frac{1}{1000}$ of an inch [illegible] × [illegible]0

× [illegible]

[To face page 278.

been most conclusively demonstrated, and in all probability, they afterwards multiply and produce the "myeloid cells" which take part in the formation of walls of the cancelli, and the bony spicules in the medullary cavity, while others degenerate and only produce the marrow fat cells, as already stated. These active changes could not occur unless the bioplasts were freely supplied with nutrient matter. We find that the blood supply to the soft temporary bone is abundant. Capillary vessels are indeed more numerous while the temporary bone is undergoing disintegration than they are in the original cartilage.

It will no doubt have occurred to the reader to ask if *every* cell in the temporary cartilage and in the ossifying fibrous matrix is represented by a lacuna in the perfect bone? From what I have seen I think it probable that, as a general rule, this is the case; but it is quite possible, as indeed occurs in cartilage, in tendon, and in muscular fibre, that some of the "nuclei" situated at the greatest distance from the nutrient surface may gradually undergo transformation into the formed material, with the exception of a very small portion of bioplast matter which dies and leaves a small space occupied with fluid. In this case these particular bioplasts would be obliterated, and would not be represented by lacunæ.

Of the formation of the Medullary Cavity, and its contents.— Amongst the pulpy germinal matter occupying the crypts of the temporary bone, capillary vessels which were to be detected in very small number prior to calcification increase considerably, and it is not unlikely that the bioplasts which take up the calcareous material may transfer it to the blood circulating in the vessels. Or, on the other hand, it may be retained by the bioplasts for a time until required again for the development of the permanent bone which is being formed beneath the periosteum. However this may be, there is no doubt about the fact that the temporary bone is removed, and that the little bioplasts are the agents concerned in its removal.

The vessels which are developed amongst these masses, and which are formed by development from the original vessels upon the cartilage have upon their outer surface little bioplasts, of which some take part in the formation of nerve fibres, while others are concerned in the production of connective tissue

which exists in a small quantity in every part of the medulla. Thus is formed that vascular membrane which lines every part of the inner surface of the bones, known as the medullary membrane, from which offsets pass and ramify amongst the medulla, and line all the cancelli of the cancellated structure of the extremity of the bones. The bioplasts remaining between the vessels, and in the reticulæ, formed by the arrangement of the medullary membrane, undergo further change. Some increase in size and form soft fatty matter, which continues to accumulate until an ordinary fat vesicle results, the development of which is described in page 300. Others grow and multiply, forming little collections varying much in shape and size, which have been already described as *myeloid cells*, fig. 185, pl. XIX. The term "cell" is however inappropriate, seeing that they are destitute of anything like a cell-wall, while many are much elongated, and form plates, processes, spicules, or branching threads. These undergo change, and a matrix is developed, in which calcareous matter is at length deposited, and the walls of cancelli and bony spicules result. Lastly, some of the bioplasts which originally occupied the medullary cavity of the bone die, and disappear altogether.

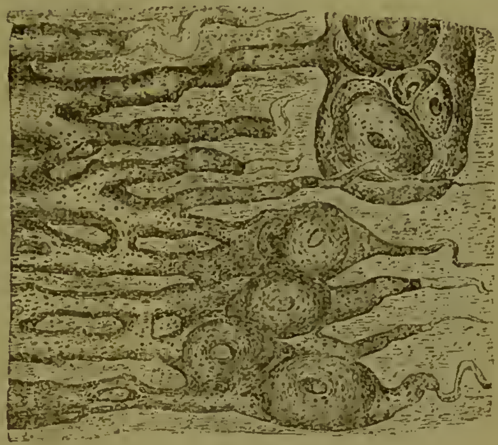
Of Ossification as it proceeds in the fibrous membrane of the Cranial Bones.—As the changes which result in the development of permanent bone beneath the periosteum, after the removal of the temporary bone, exactly accord with those which occur when fibrous tissue is converted into bone primarily, it will be well to describe this latter process in the first instance.

The bones of man, not represented at an early stage of development by temporary cartilage, which in its turn is converted into a soft spongy form of bone, are the flat extended portions of the cranial bones; for instance, the parietal, frontal, and the expanded portion of the temporal and occipital. The only bones and parts of bones of the cranium existing originally as cartilage, are the base of the occipital, the sphenoid, except the external pterygoid plate, the mastoid and petrous portions of the temporal, the ethmoid, the inferior turbinated bones, the ossicles of the ear, and the hyoid bone.

The flat bones at first appear to be composed of a form of tissue closely allied to fibrous tissue. This membranous structure grows at the edges, just as the cartilage increases at the

edges of the cranial bones of the frog. Thus the gradual increase in the size of the flat cranial bones is provided for, fig. 177. The deposition of the calcareous particles in the matrix between the masses of bioplasm, their gradual encroachment upon these, and the formation of the canaliculi and lacunæ have been fully discussed; nor do the changes which occur during the development of these bones differ in their nature from those which may be observed in the process of ossification, as it occurs in some of the fibrous tissues, in old age, or in certain morbid growths. The process of formation of lacunæ may indeed be more easily investigated as it proceeds during the ossification of the fibrous walls of certain cysts, than in normal bone.

Fig. 186.



Ossification in fibrous membrane. From the parietal bone of the fœtus at the eighth month. Human subject. × 15. The gradual extension of the bone tissue into the fibrous membrane is well seen towards the right of the drawing. The mode of formation of cancelli, and their transition towards Haversian systems is well seen in the drawing.

Of the production of secondary or permanent bone.—While the changes already described, which result in the removal of the temporary bone are proceeding, bone development of a different kind is slowly progressing beneath the periosteum, where a thin cylinder of osseous tissue, the future shaft or diaphysis of the long bone is formed. This grows in thickness by the development of new bone upon the *outer* surface in the manner discovered by Duhamel, and described in page 284.

The minute changes which take place in the development of the permanent bone beneath the periosteum were first described by Messrs. Tomes and De Morgan in their well-known memoir.* As there are several points of detail which the writer of this chapter has since succeeded in determining, a short account of the processes as observed by him will be given. In the main, this will be found to accord with the description

* Philosophical Transactions, 1853, vol. i., p. 109.

given by the distinguished authors above named. The formation of the matrix of the permanent bone' beneath the periosteum of the young animal takes place as has been already described in page 269, and it becomes calcified in the same manner, each little bioplast separating from its neighbours, while the formation of matrix proceeds upon its surface, and accumulates between the neighbouring bioplasts. When the formation of matrix is complete, calcareous particles are deposited midway between adjacent bioplasts, which gradually become encroached upon, and are at length enclosed in the spaces or lacunæ in the manner described in pages 248 to 254, and represented in the drawings, figs. 149, 150, and 151, pl. XVII, from the frog.

Fig. 187.

Section from the diaphysis of the metatarsus of the calf, after Kölliker To show the mode of development of permanent bone beneath the periosteum, as described by Messrs. Tomes and De Morgan. *a*, periosteum; *b*, tissue, undergoing ossification; *c*, spicules of bone, which, as they grow gradually encompass a vessel which becomes the Haversian vessel; *d*, completely formed Haversian systems. × 45.

The vessels beneath the periosteum are at length enveloped as it were by folds of the bone-forming bioplasts, which gradually encroach upon them until the vessel is completely surrounded. It now occupies the centre of a cylinder of bioplasts, the growth of which proceeds until a layer of some thickness is formed. At the outermost part of the soft cylinder ossification commences, and proceeds lamina within lamina until the formation of the Haversian system is complete, fig. 187. New Haversian systems are formed circumferentially beyond them until the bone has reached its permanent diameter.

The minute changes which occur have been carefully studied in well-prepared specimens taken from the growing scapula of the human fœtus at the fifth month of intrauterine life, and accurate drawings have been made from two of these specimens. The appearances observed are represented in figs. 183 and 184, pl. XIX, under a magnifying power of three hundred diameters. The changes will be understood if the reader will attentively examine the illustrations, and a more correct idea of the process will be formed than would be afforded by a minute and necessarily tedious description of the changes which take place.

Growth of Bone.—But it must not be imagined, that when bone is once deposited in a certain form, it thenceforward permanently maintains its original form and size. In the *first* place, a most important process of growth is continually going on *in the cartilage*, especially near the surface, by the multiplication of the cells; and, in the latter situation, by the increase in their dimensions already described (page 276, pl. XIX, fig. 182). In the long bones this takes place chiefly in the longitudinal direction which is that in which growth is most active; and it continues, till adult age. This fact has been long ascertained, though its real purpose appears to have been overlooked. Hales and Hunter both inserted metallic substances along the shaft of a growing bone, in a young animal, at a certain distance apart, and found, after an interval of time, that the distance between them remained the same, or nearly so, while the extremities of the bone were much further apart, thus proving that the principal growth had taken place near the extremities.

Secondly, bones increase in dimension by an accession of new *osseous* substance on their exterior, this new substance consisting not merely of new laminæ, but of new systems of laminæ, and of new involutions of the vascular surface to form new Haversian canals, so that the earlier systems of laminæ are covered over by the more recent ones, see fig. 187. But before the observations here recorded, were made, the fact had been proved by experiments with madder. It was ascertained accidentally by Belchier that the rubia tinctorum, or madder, mixed with the food of pigs, imparted its red colour to their bones, and this circumstance has been ingeniously taken advantage of by several physiologists in the prosecution of researches on the growth of bone.* Duhamel, Hunter, and

* The colouring of bone by madder results from an affinity of the colouring principle for the phosphate of lime. This opinion was distinctly broached by Haller (El. Phys. t. viii. p. 329), and it was subsequently proved by Rutherford, who shewed it experimentally. To an infusion of madder in distilled water add calcic chloride : no change takes place. Then add sodic phosphate in solution. By double elective affinity calcic phosphate and sodic chloride are formed. The phosphate is insoluble, and subsides in union with the colouring matter as a crimson lake. When madder is given as food, its colouring principle is absorbed, and circulates with the blood ; and it colours first that part of the bone which is in course of formation from that fluid, or which has been last formed, *i.e.*, which is nearest the vascular surface.

many others, have performed multiplied experiments of the kind. In the museum of King's College are some good preparations of bones so acted upon. It is found that, in very young animals, a single day suffices to colour the entire skeleton, apparently in an uniform manner; in these there is no osseous material far from the vascular surface. But, if we make a transverse section of one of the long bones so treated, we observe the deepest, or even the only colour, to be really on the vascular surface; the Haversian canals are each encircled by a crimson ring. This beautiful illustration is due, as far as we know, to Mr. Tomes, who has long possessed some very elegant specimens prepared in this way.

In full-grown animals the bones are very slowly tinged, because the great mass of the bone is not in contact with blood-vessels; each Haversian system, for example, has only its small innermost lamella in contact with them, and besides, the osseous matter is altogether more consolidated and less permeable by fluids than at a very early period of life. In the bones of half grown animals a part of the bone is nearly in the perfect condition, while a part is new and easily coloured. Hence, it is easy in them to distinguish the new from the old by means of madder.

Now, madder given to half-grown animals colours the long bones most deeply in the interval between the shaft and extremities, and on the surface of the shaft, immediately beneath the periosteum, where the most active changes are proceeding. When madder is given at intervals, the tints in the bone are interrupted, the layers in course of formation during its administration are coloured, while those formed during the intervening periods are colourless. The long period during which bones retain the madder tinge, shews that the colouring matter is not readily resumed by the blood, from its combination with the calcic phosphate.

Perhaps few questions have more divided the minds of physiologists than that regarding the share taken by the periosteum in the growth and regeneration of bone, for these last are essentially the same process. Duhamel placed a ring of silver round a bone of a young pigeon, without injuring the periosteum. After some time, during which the bone had increased in diameter, he found the ring in the medullary canal, which had acquired a capacity equal to the previous diameter

of the whole shaft. In this case, the first effect is upon the periosteum which cannot grow where it becomes tightly grasped by the ring. Immediately beyond the foreign body there is, however, redundant growth, and the sub-periosteal bone-forming texture increases in amount, and gradually overlaps the ring which is after a time embedded in the newly-formed bone.

Fig. 188.

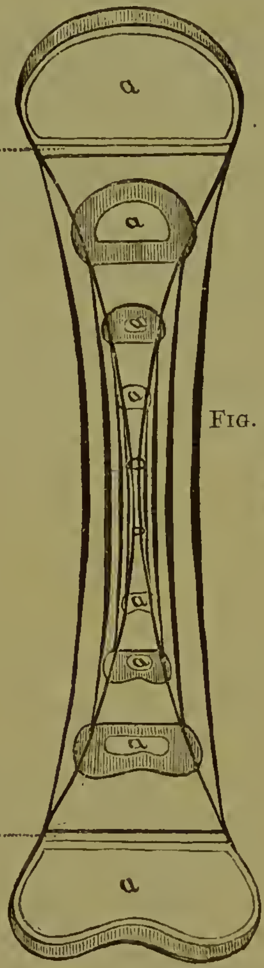


Fig. 188*a*.

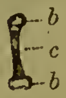


Diagram to show the mode of growth of a long bone. Fig. 188*a*. The bone of the natural size soon after commencement of ossification. *b b*, Epiphyses; *c*, Shaft or Diaphysis; *d*, layer of cartilage between the epiphyses and diaphysis, which is the last to undergo ossification. The change in outline of the shaft at different stages of growth is seen, and the lines prolonged from the shaft of the youngest bone to the epiphyses of the latest indicate the form which the bone would have assumed had growth taken place at the extremities of the shaft only, and not beneath the periosteum. Altered from Kölliker and others.

In early life the cancelli are small, and there is no medullary cavity. Gradually the cancelli enlarge, and those within the shaft blend more and more with one another, by the removal to a greater or less extent of the intervening osseous walls, until at length a medullary canal is formed, around which the cancelli are very open, large, and irregular. This augmentation of the vascular cavities of bone is attended with a development of adipose vesicles and their capillaries in the new space. The fat contained in the medullary canal gradually accumulates so much, that a special artery becomes enlarged to supply it, assuming the very inappropriate title of "*the* nutrient artery of the *bone*."

Of the changes in form which occur during growth of a long bone in length and circumference.—The long bones grow in length by the formation of new cartilage cells at the point where the shaft (diaphysis) joins the "*epiphysis*" *dd*, fig. 188. The cartilaginous portion of each "*epiphysis*" increases in all directions by the formation of new cells at every part of its circumference, and by the slow multiplication of those already produced. The central part of the shaft (diaphysis) of a growing

long bone, midway between the growing extremities, is clearly the part which was first formed, or the oldest portion of the shaft. The oldest part of an epiphysis must be the centre.

The several stages through which a long bone passes during its growth will be understood if fig. 188 be carefully examined. In each of the outline figures *a* represents the ossific centre of the epiphyses, and the lines prolonged from the extremities of the largest bone indicate the form this would have had in its fully developed state had growth taken place at the extremities of the shaft only, and no provision been made for its increase in diameter by the development of new bone, layer outside layer, around the entire circumference of the shaft beneath the periosteum, as has been described in page 282.

Reparation of Bone.—The great importance of this subject to the surgeon has led to many very interesting researches from the time of Duhamel to the present day, and by these the several steps of the process by which new bone is deposited have been ably elucidated in all that relates to their more obvious characters. When a fracture occurs, blood is, of course, effused into the wound, both from the ruptured vessels of the bone itself, and from those of the surrounding structures participating in the injury. This blood soon undergoes change. Its colouring matter is absorbed, and its bioplasm particles (white blood corpuscles) multiply. The fibrin at length disappears, being appropriated by the developing bioplasts, and in its place a form of fibrous tissue is produced. This at length undergoes calcification, and from the fourth to the sixth week a soft temporary bone, termed by Dupuytren *provisional callus*, results. This is slowly replaced by the development of permanent bone (*permanent callus*) from the growth and mutiplication of the bioplasts of the torn periosteum of the original bone.

The spongy temporary bone invests the exterior of the broken extremities, and extends between them in the form of a case, by which they are firmly held together. If the medullary canal has been broken across, and the broken ends evenly adjusted, there will be likewise an interior stem of new bone connecting the medullary canal of the fragments in the axis of the bone; the opposed surfaces of the compact tissue being as yet ununited. It would appear that new bone is formed more

exuberantly in the situations of the provisional callus because of their greater vascularity, just as we may suppose the function of ordinary nutrition to be more active in those parts than in the compact tissue of the bone. The permanent callus has all the characters of true bone.

When the reparative process in bone is interfered with, either by mal-apposition of the fragments, or by constitutional fault, a spurious union may occur by the medium of a ligamentous substance, or even a diarthrodial joint may be formed at the seat of fracture. The ends of the bones become altered in form and adapted to one another, a kind of false capsular ligament is developed, and sometimes even an imperfect cartilage, and a lining membrane furnishing a lubricating fluid.

Of Inflammation of Bone, of Caries and Necrosis.—In the development of bone, in the removal of old Haversian systems, and in the formation of new ones, in the union of fractured ends of bones, in caries, and in the formation of bone cancer, the bioplasts or masses of living germinal matter are the active agents. If bone is to be *absorbed* these little masses of germinal matter multiply very rapidly and increase at the expense of the surrounding bone. On the other hand, if bone is to be *formed*, it has been shown that the masses of bioplasm having increased in number for a time, cease to multiply, but each increases in size, and the outer part of each slowly undergoes conversion into formed material, which in its turn becomes gradually impregnated with hard calcareous salts. The harder the bone is to be, the slower must this process proceed.

In inflammation of bone the bioplasts of the lacunæ increase in size, and appropriate the formed material adjacent to them. Thus, a lacuna becomes much enlarged, and is found to contain several small spherical masses of bioplasm instead of one (Pl. XVII, fig. 156, page 250). The bone tissue between several lacunæ may be disintegrated and removed, and thus a space of considerable extent may be scooped out even in the compact tissue, and may be occupied by masses of bioplasm, resulting from the division of those belonging to several lacunæ. This is one way in which an abscess in bone may originate.

In *rickets*, *caries*, and *cancer*, the vital changes going on in osseous tissue are much more active than in healthy bone which lives and grows but slowly in comparison. In these mor-

bid processes the bioplasm increases too fast, and the condensation of the tissue which is requisite for the production of true bone does not take place. Here, as in all other cases, rapid change is associated with brief duration, while the well-developed normal lasting tissue is formed very slowly, and the changes succeed each other in the most gradual, orderly, and regular manner.

In caries, the bioplasm of a part of a bone receives too large a supply of nutrient matter, it grows too fast, and lives upon the surrounding tissue which has been already formed.

In necrosis, the death of the bioplasm of many lacunæ takes place. It is easy to conceive that such a result must ensue if the supply of blood be cut off, for the currents of fluid, which during life flow through the canaliculi, and permeate every part of the bone, cease, and the bioplasts die. Changes in the small trunks which supply the Haversian vessels, ending either in their obstruction, as, for example, by clots, or their obliteration by pressure, exerted upon them, as from the growth of adventitious tissue around, may cause necrosis of a considerable extent of osseous tissue. Thus effusion into the deeper and more spongy portion of the periosteum, as occurs in the formation of a node, may cause the occlusion of some of the vessels passing from this membrane into the compact tissue. The passage of blood through these vessels being interfered with, the bioplasm of all that portion of bone receiving nutriment from them must die, and a piece of bone of considerable size may become "necrosed." Immediately around this the nutrient matter would flow more freely, but of course less regularly. In consequence the bioplasm of the neighbouring lacunæ would grow much faster, and thus a vast number of bioplasts would result. These would even eat away, as it were, but of course very slowly, the dead bone, which soon becomes surrounded by them. After the bioplasts have accumulated to a certain extent, many increase in size, produce formed material, which in its turn ossifies, and thus the piece of dead bone is at length embedded in new irregularly formed bone. This process goes on, unless the whole of the dead bone (sequestrum) is removed by the process above referred to, or by surgical interference. Before the dead bone can be removed by the surgeon, he has in many cases to cut away very much of the new bone

which has been produced. Now, it has been said that the dead bone acts as an irritant—as a foreign body—and that this is the reason why the bone increases around it. Such a doctrine is still strongly maintained, although no one has been able to show exactly what is meant by the supposed "irritation." It has been assumed that an irritant or excitant is always necessary to increased action, that by this "irritant" the living cells are "excited" to live faster than usual. But for this increased activity all that is really required is *a more free access of nutrient matter*. The so-called "irritant," instead of "exciting," acts in the most passive manner possible. It allows pabulum to have freer access to the living bioplasm. By it the restrictions under which growth normally takes place are to some extent removed. There is no "excitation to increased action" at all. The more freely living matter is supplied with pabulum the faster it grows. "Increased action" in a living structure results from the *removal of restrictions*, as occurs when the *rupture*, *perforation*, or *softening* of the "cell-wall" or "intercellular substance," takes place. The nutrient pabulum comes more readily into contact with the bioplasm which grows faster, but not in consequence of "*stimulation*," "*excitation*," or "*irritation*."

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CHAPTER VII.

OF ADIPOSE TISSUE.—THE ADIPOSE VESICLE.—VESSELS OF ADIPOSE TISSUE.—OF FAT.—DISTRIBUTION OF ADIPOSE TISSUE.—ORIGIN AND PRODUCTION OF FAT.—OF THE REMOVAL OF ADIPOSE TISSUE, AND THE ABSORPTION OF FAT.—ABNORMAL DEVELOPMENT OF ADIPOSE TISSUE.

THIS tissue has no alliance either of structure, function, or composition with the areolar tissue, but it is usually associated with it. Malpighi, W. Hunter, Monro, and, more recently, other distinguished anatomists, have pointed out the distinctness of these two tissues. Adipose tissue may be very rapidly formed and removed. It may be regarded as one of the lower simpler tissues of the body. An individual may experience the greatest alterations in regard of the amount of adipose tissue in his organism, and change may even occur several times during life, without any serious derangement of the health being necessarily occasioned. This tissue is found in connection with many textures of the body besides the areolar or connective. Bone, glandular organs as the mammary glands, the liver, and pancreas usually exhibit more or less adipose tissue. A common use of this tissue being to occupy spaces of various dimensions left in the interstices between organs, and thus to facilitate motion and contribute to symmetry, it is very commonly closely associated with the areolar tissue; but the connection is not an essential one.

In the cancelli of bones there is a large deposit of fat, but no areolar connective or filamentary tissue; and in numerous situations, as the eyelids, beneath the epicranial aponeurosis, between the rectum and bladder, under the mucous membranes, and in the whole of the cutis, the areolar tissue exists without being ever accompanied by fat.

A distinction is to be drawn between the fat and the adipose tissue. Under the latter head may be comprised a greater or less proportion of areolar tissue (in the meshes of which the adipose vesicles with their contained fat are situated), vessels, which ramify very freely, and a few nerve fibres distributed to the

latter. The *fat* is the material contained within the vesicles, fig. 189.

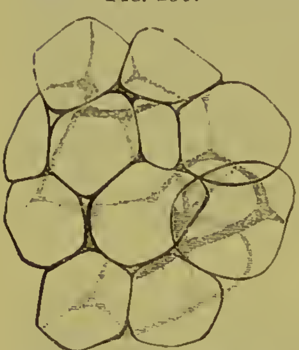
The *Membrane of the Adipose Vesicle* does not exceed the $\frac{1}{20000}$ of an inch in thickness, and is quite transparent. It is moistened by watery fluid, for which, as Mr. Paget has suggested, it has a greater attraction than for the fat it contains. It is perfectly homogeneous, having no appearance of compound structure, and consequently belongs to the class of simple or elementary membranes. Each vesicle is complete in itself; is from the $\frac{1}{300}$ to the $\frac{1}{800}$ of an inch in diameter, when fully developed; and is supplied on its exterior with capillary blood-vessels, having a special disposition. When the fat of adipose tissue is absorbed, the vesicles shrink somewhat but remain, and it is probable that fatty matter may be removed from and subsequently be deposited in the very same fat vesicle.

FIG. 189.

A fat cell after Schwann, showing the bioplasm or nucleus, *d*, and the membrane, *c*

The fat vesicles are usually found in great numbers together, and as they increase in dimensions they become flattened on their contiguous aspects, and assume a polyhedral figure more or less regular, as may be noticed in ordinary suet, fig. 190. But, if isolated, their form is rounded, as may be seen in eminent beauty in the double series of them which frequently accompanies the minute vessels traversing membranous expansions of the areolar tissue, and other structures, particularly the mesentery of small animals. The vessels are thus attended by fat vesicles, for the manifest purpose of protection from the pressure to which they would be exposed in their open course, and they throw around each vesicle a capillary loop, fig. 194, pl. XX.

FIG. 190.



Fat vesicles, assuming the polyhedral form from pressure against one another. The capillary vessels are not represented.—From the omentum; magnified about 300 diameters.

Where the adipose tissue is in considerable quantity, it is commonly subdivided into a number of small fragments or lobules, fitted accurately to one another and invested with areolar tissue, for the purpose, chiefly, of permitting motion

between the parts of the mass, but, also, for the convenience of the distribution of its blood-vessels.

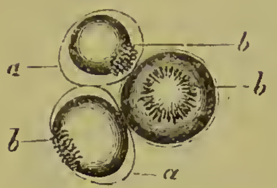
Vessels.—In fig. 194, pl. XX, the vessels of a lobule of adipose tissue are represented, the artery being coloured red and the vein blue. The blood-vessels enter the chinks between the lobules, and are soon distributed through their interior, under the form of a solid capillary network, whose vessels occupy the angles formed by the contiguous sides of the vesicles, and anastomose with one another at the points where these angles meet. This is one of those situations where the capillary vessels can be most unequivocally proved to possess distinct membranous parietes.

Fat is a white or yellowish soft substance, exhibiting no structure whatever, entirely unorganized. The chemical composition of fats has been very carefully studied, but there is still some difference of opinion among chemists concerning the exact nature of the components of fat. By decomposition fatty acids, principally palmitic, and stearic, may be separated from human fat. These were in combination with glycerine to the elements of which they seem to have been united as to an organic base. By boiling oil or fat with a solution of caustic alkali, the acids unite with the potash, forming soap, and the glycerine remains dissolved in the liquid. By evaporating this liquid (in which any excess of alkali had been previously neutralized by tartaric acid) to a thick syrup, the glycerine may be separated from it by solution in strong alcohol, but this substance is now obtained by another process in an exceedingly pure state. It is manufactured upon an enormous scale by Messrs. Price and Co., and is much used. Its value as a medium for preserving microscopical preparations is great. See page 58.

We may often detect a spontaneous separation of the crystalline from the oily fat within the fat vesicle of the human subject. The solid portion collects in a spot on the inner surface of the cell-membrane, and looks like a small star, fig. 191, *b b b*. The elaine occupies the remainder of the vesicle, except when the quantity of fat in the cell is smaller than usual; in which case we may often discern a little aqueous fluid between the elaine and the cell-membrane on the side farthest from the star (fig. 191, *a a*); a condition, by the way, which is very

favourable for the demonstration of the membrane itself. The fatty matter contained in the fat vesicle, even in the case of very hard fats like suet, is always in a soft liquid state while the body is alive.

Fig. 191.

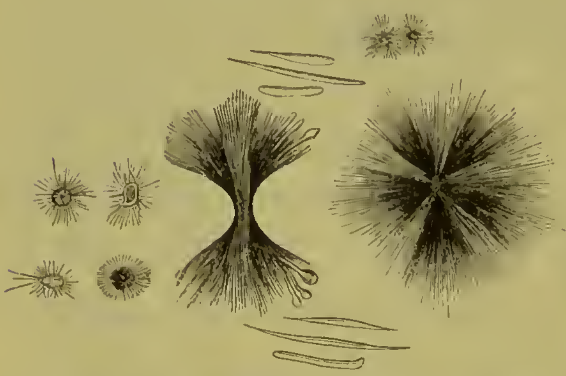


Fat vesicles from an emaciated subject:—*a a*, the cell-membrane; *b b b*, the solid portion collected as star-like mass, with the elaine in connection with it, but not filling the cell

The softer kinds of fat were denominated by the older anatomists *pinguedo*, lard; and the more solid *sebum* or *sevum*, suet, tallow. Hunter distinguishes four varieties as to fluidity; oil, lard, tallow, and spermaceti. The elaine of human fat retains its fluidity at 40° F. Lard melts at 86° F. Tallow at 104° F. Spermaceti is fluid in a heat above 115° F., and solid at 112°. Oil is elaine with little or no stearine, as the neat's foot oil, obtained from the bones of the ox. In lard, the stearine is in abundance, but the elaine slightly predominates. In tallow there is a predominance of stearine.

Heintz showed that human fat contained tripalmitin, from

Fig. 192.



Stearine.

Fig. 193.

Stearic Acid.

After Robin and Verdeil.

which palmitic acid may be obtained by saponification. The other constituents of human fat are stearine and elaine. The acids are the *palmitic*, *stearic*, and *oleic*. The composition of the fatty constituents in human fat is as follows:—Tripalmitin, $C_{102}H_{98}O_{12}$, which corresponds to three equivalents of palmitic acid 3 $(C_{32}H_{32}O_4)$ + one equivalent of glycerine $(C_6H_8O_6)$ − 6HO. Tristearin, $C_{114}H_{110}O_{12}$, which represents three equiva-

lents of stearic acid ($C_{36}H_{36}O_4$) + one equivalent of glycerine ($C_6H_8O_6$) − 6HO. Triolein, $C_{114}H_{104}O_{12}$, which corresponds to three equivalents of oleic acid ($C_{36}H_{34}O_4$) + one equivalent of glycerine ($C_6H_8O_6$) − 6HO. Human fat according to Chevreul, consists of

Hydrogen	..	..	11·416
Carbon	..	..	79·000
Oxygen	..	..	9·584
			100·000

Distribution.—The adipose tissue is met with very extensively in the animal kingdom. It is found in larvæ as well as in the perfect insect; also in the mollusca. It prevails in all the tribes of the vertebrata. In fish it occurs throughout the body; but in some, as the cod, whiting, haddock, and all of the ray kind, according to Hunter, it is only met with in the liver. In reptiles it exists chiefly in the abdomen. In the frog, toad, &c., it is found in the form of long appendages, something like the appendices epiploicæ of man, situated on each side of the spine. In birds, it exists chiefly between the peritoneum and abdominal muscles; but there is also a considerable deposit in the bones of the legs, feet, last bones of the wings, and of the tail, especially of the swimming tribes, the oily principle being more abundant than in mammals. In mammalia it is very generally diffused. This class, as a whole, has the greatest quantity under the skin, and about certain of the abdominal viscera; but the hare forms a remarkable exception, it being sometimes difficult to find a particle of adipose tissue in the whole body. It usually abounds most in the beginning of winter; and this is especially the case with the hog, and with hybernating animals, which, during their dormant state, absorb it into the system.

It is ordinarily accumulated in large masses about the kidneys, more particularly in ruminants, where it furnishes the best example of that variety of adipose tissue termed suet.

Among mankind many remarkable varieties exist as regards this tissue. In general, women are fatter than men. The healthy human fœtus, after the middle of the period of gesta-

tion, accumulates fat in considerable quantities; towards middle age, there is a similar disposition, which has not escaped ordinary observation, "Fat, fair, and forty." In old age and decrepitude, the adipose deposit greatly diminishes.

Differences are also constantly seen in individuals, which can be referred only to an original constitutional bent. Thus young children are occasionally so overloaded with this tissue as to be unable to follow their sports; and it is not uncommon for a similar tendency to manifest itself towards the adult period, particularly in girls. In elderly persons, fat is especially prone to be accumulated over the abdomen, and between the layers of the epiploön and mesentery. Instances where it attains the thickness of three or four inches under the skin of the belly are not unfrequent in corpulent persons. A similar abundance occasions the "double chin." On the other hand, there are certain individuals who cannot be made fat. No matter in what manner the diet may be changed in quantity or quality, there are persons whose adipose tissue cannot be increased.

It is perhaps possible for the body to grow so egregiously fat as to become lighter than water; but whether implicit faith is to be placed in the story of the Italian priest Paolo Moccia, who weighed thirty pounds less than his bulk of water, and therefore could not sink in that fluid, we do not pretend to decide. The excessive deposit of this substance constitutes a disease, which has been not very correctly called polysarcia. John Bull is celebrated for his proneness to accumulate fat; M. Blainville remarks, with *naïveté*, "We have seen many individuals of the English nation whom *embonpoint* had rendered almost monstrous; and I remember among others, a man exhibited at the Palais Royal who weighed five hundred pounds. He was literally as broad as he was long." But this tendency is by no means peculiar to Englishmen.

Among the Hottentot women, the fat is apt to gather in the buttocks, and is considered a prominent mark of beauty; but this does not usually occur till after the first pregnancy. A somewhat analogous formation exists in a variety of sheep,* reared by the pastoral tribes of Asia, in which a large mass of fat covers the buttocks and takes the place of the tail, appear-

* *Ovis steatopyga*, fat-buttocked sheep. Pallas.

ing when viewed from behind as a double hemisphere, in the notch of which the coccyx is buried, but is just perceptible to the touch. These protuberances, when very large, fluctuate from side to side, and sometimes attain the weight of thirty or forty pounds. The quantity of fat in a moderately fat man is estimated by Béclard at about the twentieth of the weight of the body, but in many it amounts to much more.

Fat is found in the following situations in the human body; in the orbits, in the cheeks, the palms of the hands and soles of the feet, at the flexures of the joints, and between the folds of the synovial membranes of joints, around the kidneys, in the mesentery and omentum, in the appendices epiploicæ, on the heart, in the subcutaneous layer of areolar tissue, but especially that of the abdomen, and of the mammary region, and in the cancelli and canals of the bones forming the medulla. It never occurs in the areolar tissue of the scrotum and penis, or of the nymphæ, nor in that between the rectum and bladder, nor along the median line beneath the skin, nor in sundry other situations.

Fat is found in the liver even in health, and a large quantity may be obtained from the brain and nerves. In these organs it is not enclosed in vesicles of delicate membrane, but is associated with the matter of the tissues themselves. Oily matter exists in greater or less proportion in all the textures of the body, from which it may be extracted by alcohol and ether, although not a trace can be detected by microscopical examination. See page 146. Even the transparent fluids of the organism are not destitute of fatty material, and, as is well known, the chyle contains a very considerable proportion.

Origin and Production of Fat.—There can be no doubt that fat is derived from the blood. All the most recent analyses of that fluid assign to it a certain proportion of both the crystallisable and the oily portion of the fat; according to Lecanu, about four parts in a thousand. In many instances, the fatty matter accumulates in the blood; cases of which have been recorded by Morgagni, Hewson, Marcet, Traill, and Babington. In such cases the serum is opaque and nearly as white as milk, and, on standing a short time, a film forms on the surface like cream. On the addition of ether, the creamy pellicle is dissolved, and the serum loses its opacity. M. Blainville relates, that, in

dissecting the last elephant that died in the Jardin des Plantes, he happened to wound the jugular vein, and the next morning he found that the stream of blood, which flowed from the vein, had deposited on each side a considerably quantity of a free fatty matter, which on analysis he found to have exactly the composition of ordinary fat. A similar fact may be often observed in the blood from slaughtered animals, which we find to be sometimes loaded with fat.

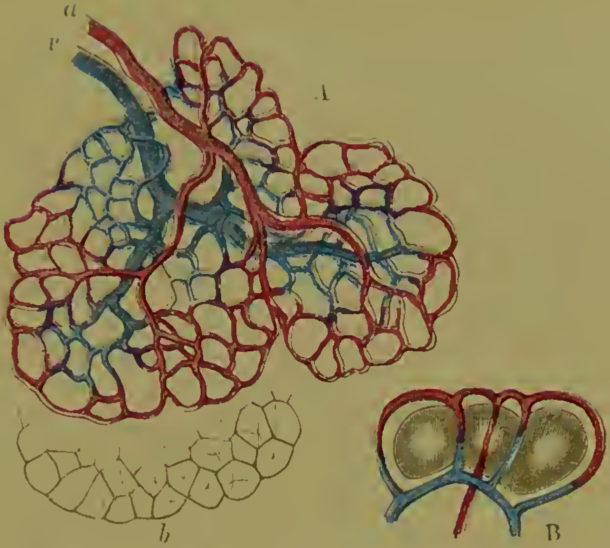
From what source is this fatty material furnished to the blood? Mainly, no doubt, from fatty matters introduced into the system in the food, whether animal or vegetable substances, but fat may be formed, and in considerable quantity, from nutrient materials which do not contain it. From many non-nitrogenized articles of diet, starch, gum, sugar, alcohol, beer, fat may be formed, and in large quantity, by the agency of the bioplasm of the body. From the constituents of meat and other nitrogenous foods, fat may also be formed in the organism.

If the system be imperfectly supplied with oxygen, while organic compounds containing carbon are furnished to it in considerable quantity, the most favourable conditions will exist for the development of fat. On the other hand, exercise and labour, which increase the supply of oxygen, diminish or prevent the formation of fat. "The production of fat," says Liebig, "is always a consequence of a deficient supply of oxygen, for oxygen is absolutely indispensable for the dissipation of the excess of carbon in the food. This excess of carbon, deposited in the form of fat, is never seen in the Bedouin or in the Arab of the Desert, who exhibits with pride to the traveller his lean muscular sinewy limbs altogether free from fat; but in prisons and jails it appears as a puffiness in the inmates, fed, as they are, on a poor and scanty diet; it appears in the sedentary females of oriental countries; and, finally, it is produced under the well-known conditions of the fattening of domestic animals."*

A good illustration of these views is afforded by the carnivorous animals. In the wild state, living entirely on azotised food, and enjoying abundance of air and exercise, they are lean; but, when domesticated, living on a mixed diet, taking

* Liebig's Organic Chemistry.

Fig. 194.



...vessels of adipose tissue. Artery red. Vein blue. A is a minute lobule in which the vessels only ... *a*, terminal artery. *v*, the primitive vein. *b*, fat vesicles at edge of a lobule as seen in an uninjected specimen. × 100.
... of the arrangement of the capillaries around the vesicles, more highly magnified. p. 293

Fig. 195.

...tive tissue corpuscles in ... fatty matter is being deposited *a*. The latter in some ... increases until a body ... results × 215 p. 303.

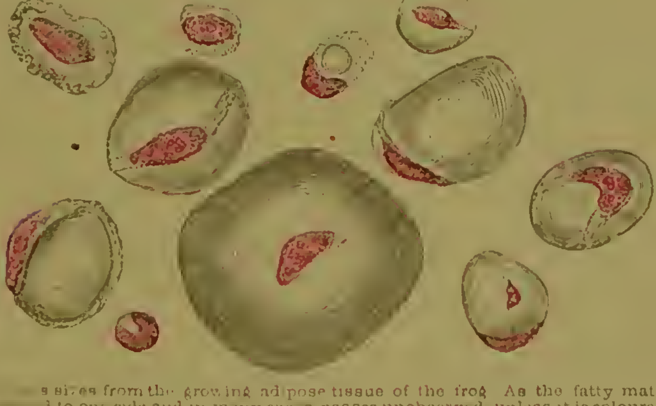
Fig. 196.

Fat bioplasts from the frog showing the mode of formation of the oily matter. The youngest one is at the top. The vesicle is so thin as to be not yet visible. × 700. p. 300

Fig. 197.

Cartilage from the ensiform cartilage of a young white mouse, showing the deposition of fatty matter in the bioplasm. × 700 p. 302.

Fig. 198.



... sizes from the growing adipose tissue of the frog. As the fatty matter accumulates, ... to one side and in many cases passes unobserved, unless it is coloured. × 215 p. 303.

$\frac{1}{1000}$ of an inch — × 215. $\frac{1}{1000}$ of an inch ———— × 700.

[To face page 293.

little exercise, and being imperfectly supplied with oxygen, they grow fat.

In animals that hybernate, fat is deposited in enormous quantity just prior to the hybernating period, and during that time it gradually disappears, supplying nutriment to the system, and carbon for the respiratory process. These facts were clearly ascertained in hedgehogs by the celebrated Dr. Jenner.

It is generally admitted that the disintegration of fat is attended with the development of heat, the oxygen uniting with the carbon, an amount of heat is generated proportionate to the quantity of carbonic acid formed. But it may be fairly questioned whether the high temperature of the body can be thus explained, seeing that in many conditions in which the temperature rises many degrees within a very short period of time, the oxidising process is completely at fault, and the quantity of oxygen consumed is far less than in health. Although ordinarily much fatty matter is concerned indirectly in the changes which take part in the development of animal heat, the large amount of fat existing in every form of nerve tissue clearly shows that the action of the nervous system so essential to the maintenance of life is in some way dependent upon the due supply of a sufficient quantity of nutrient material containing the elements from which fat may be formed.

Lastly, fat being a bad conductor of heat, is useful for retaining it in the bodies of animals. Those animals that have little hair on their skins, and are at the same time exposed to the influence of extreme cold, have a great quantity of subcutaneous fat. This is remarkably the case in the whale tribe, most of which have a thick layer of adipose tissue (blubber) between the smooth bare skin and the muscle beneath. In man, the subcutaneous fat, which is so generally met with, even in apparently lean subjects, is doubtless a most valuable protection against the cooling effects of arctic cold.

The Development of Adipose Tissue.—The process of formation of adipose tissue may be studied in the embryo of any vertebrate animal. Long before fat is actually produced, the embryonic matter (bioplasm) which is to take part in its formation can be distinguished from that which is to give rise to other textures. But the several stages through which adipose tissue passes in its development may be as clearly

made out in any young mammal at the time of its birth as during the earlier periods of development. And there is this advantage in conducting the examination at this later time, —that fully-formed adipose tissue may be contrasted with the same texture in its embryonic state in the same microscopic specimen, for the development of this tissue continues long after birth. Nay, in certain eases it may be studied in an embryonic condition even in the adult. Thus we have obtained exeellent specimens which illustrate every stage of the process, taken from the fully formed frog. Pl. XX, figs. 196, 198. Indeed, in hybernating animals *new* adipose tissue is formed just prior to each recurrent period of hybernation, but it is probable that in some instances fatty matter is also reformed in the very same old cells from which it had been previously removed.

It would be supposed that a tissue which altered its volume so quickly and to so great an extent as this, would have a very intimate relationship with the blood from which the elements entering into its formation are derived,—and this is the case, for adipose tissue is very largely supplied with blood, and in corpulent persons who make fat fast, the greater part of the blood of the body is probably distributed to the adipose tissue, and other tissues and organs suffer in nutrition. The muscles become weak, and waste, and the nerves are impaired.

Vessels, arteries, capillaries, and veins, are developed *pari passu* with adipose tissue. And there is not an instance among vertebrate animals of the occurrence of adipose tissue destitute of vessels. The vascularity of the medulla or marrow of bones is remarkable. The rate at which adipose tissue grows, in certain cases, is very striking, and probably the animal in which it is produced most quickly is the young pig, whose adipose tissue doubles in weight in the course of a very few weeks.

In the meshes of the capillary network of very young adipose tissue may be seen the little masses of bioplasm, which are concerned in the production of fat. These, at a still earlier period, are in contact with the external surfaee of the vascular wall. It certainly is not possible to determine by any appearanee manifested by the numerous bioplasts in the immediate neighbourhood of the vessels, which of them are to take part in the development of new capillaries, and which are to become

connective tissue or fat. The capillaries themselves multiply as the adipose vesicles grow, and the vascular network increases as in other situations, by the extension of bioplasts in a loop-like form from the capillaries already existing.

The changes taking place in the development of an individual *adipose vesicle* will be understood if figs. 196, 198, pl. XX be referred to. At first all that is to be discerned is a small oval or spherical mass of bioplasm or living matter, perfectly naked, that is, entirely destitute of a cell wall. This little bioplast usually exhibits one or more new centres of growth (nuclei) embedded in it. The formation of the fatty matter occurs in this way:—in the very substance of the bioplasm, but always outside and away from the new centre or nucleus, a little oil globule makes its appearance. It results from changes in the living matter itself. A portion of this bioplasm dies, and among the substances resulting from its death are fatty matter, which being insoluble, remains, and soluble substances which are carried away in the blood. Starch globules and other secondary deposits formed in the interior of elementary parts are produced in the same manner by the death of the bioplasm. The fatty matter does not come from the blood as fat, and deposit itself in the cell, nor is it formed by the collection and aggregation of excessively minute granules, which traverse the vascular walls suspended in serum; nor is it precipitated from the nutrient fluid after the manner of crystals. But it invariably results from the *transformation of living matter*, and different kinds of living matter, as is well known, will produce different kinds of fat. The properties and composition of fat in different animals differ, because the powers of the bioplasm or living matter of each animal are so different.

The bioplasm of the fat-cell does not diminish in proportion exactly as the oil increases, because the conversion of pabulum into bioplasm proceeds as fast as the conversion of the latter into formed material takes place, as has been already explained in page 79.

In 1861 one of us showed the relation of the oil or fat to the included nucleus or mass of living germinal matter or bioplasm, and pointed out that the fat of the fat cell and the starch of the starch cell were formed by the bioplasm itself. Nevertheless many who have written since have affirmed that

we still remain completely ignorant concerning the relation of the fatty matter to the bioplasm of the cell. By aid of the plan of preparation already referred to, the change in amount of the bioplasm and the relation of this substance to the formed fatty matter may be so distinctly determined in cells at different stages of development that not a doubt can be entertained concerning the mode of formation of the fat, and the true relation which the bioplasm bears in all cases to this substance.

The little globule of fat having been once formed in the substance of the bioplasm, pl. XX, fig. 196, may increase in size by the addition of new particles to it, until the globule becomes larger and larger, being at last, perhaps, fifty times the size of the bioplast that remains, fig. 198, pl. XX; or the number of globules may increase until a compound mass, consisting of hundreds of separate little oil globules, results. In most mammalia and man, the globule is single, but in some of the reptiles (lizard, snake, chameleon) the fat cells in many of the tissues consist of numerous separate oil globules, almost uniform in size. And in some parts of the organism of some mammalia (rat, mouse), and even in certain cases in man himself, the same fact has been noticed. In insects the "fat cells" are often of enormous size, consisting of aggregations of very small oil globules, which collect around the mass of bioplasm that has taken part in their production. In the livers of many fishes, particularly the eel, a somewhat similar arrangement may be observed. In these cases the nutrient matter passes in the interstices between the already formed oil globules to the bioplasm in the centre. The circumferential portions of the latter die, and undergo transformation into fatty matter which is deposited within that already produced. The globules on the outside of the cell or on its surface are therefore the oldest.

To recur to the development of the adipose vesicle in man. At the same time that the oil globule deposited in the bioplasm of the developing adipose tissue increases, a change of another kind is taking place upon the surface of the mass. The living matter in this situation dies and becomes changed, so as to form a delicate transparent structureless membrane, which increases in extent as its contents become augmented by the absorption of nutrient material into the included bioplasm,

and its appropriation. The so-called wall of the adipose vesicle is therefore formed in accordance with the mode of production of formed material generally. But the wall of the adipose vesicle is of excessive tenuity, and readily permeable to fluid in both directions, so as to allow for the very free passage of nutrient material to the bioplasm within and that of fluid resulting from the changes of the bioplasm in the opposite direction towards the blood. In this way the rapid increase and removal of adipose material is rendered possible.

But the mode of development of fat may be studied in other textures besides the adipose tissue itself. Thus, in connective tissue it is sometimes found that fatty matter is formed in the bioplasm of the connective tissue corpuscle, and an elementary part at length results which closely resembles an ordinary fat cell.

Some connective tissue corpuscles from the frog are represented in fig. 195, plate XX, magnified 700 diameters. In the upper one an oil-globule is seen, and in many parts of the preparation from which the drawing has been made, connective tissue corpuscles were seen which illustrated every stage of change up to the formation of a fat cell, resembling that of ordinary adipose tissue.

Some observers, indeed, consider that the adipose tissue is not a distinct texture at all, but that the fat cell is developed from the corpuscles of connective tissue—a view which is certainly erroneous, for, in many cases, at an early period of development, collections of bioplasts can be detected without difficulty, in relation with which not a trace of connective tissue can be found; while around the vessels of the mesentery of young animals the bodies in question are seen as well as the corpuscles of the connective tissue of the mesentery, but quite distinct from them. While, therefore, it is certain that the connective tissue corpuscle, the cartilage, and some other elementary parts, may be transformed into fat cells, it is also an unquestionable fact that, in the development of adipose tissue special bioplasts are concerned which are quite distinct from those engaged in the formation of connective tissue.

The bioplasm of cartilage in highly fed animals often produces oil globules which accumulate in the so-called cartilage cell, and the bioplasm becomes pushed to one side, and so

compressed that it may entirely escape notice. In the young mouse such a change is commonly observed, and, not unfrequently, the fat accumulates to such an extent that the tissue might almost be described as adipose tissue, in which the ordinary vesicle or cell wall is replaced by firm cartilaginous tissue. In fig. 132, pl. XV, is represented a small portion of the cartilage tissue of the thinnest part of the ear of a young white mouse. Each spherical capsule of cartilage tissue is occupied by a large oil globule, between which and the inner wall of the capsule the remains of the bioplasm that has taken part in the formation of both fat and cartilage may be distinctly seen if the specimen has been properly prepared by previous soaking in carmine fluid, page 60. In fig. 197, pl. XX, two "cells" from the ensiform appendix of the white mouse are figured, in which fatty matter is being formed.

That condition which is termed fatty degeneration of the liver, and which is very common in phthisis also affords a good illustration of the changes which occur when fat is formed. To such an extent does the change sometimes proceed, that a section of the fatty liver could not be distinguished from certain forms of adipose tissue. Not a particle of biliary colouring matter or other evidence by which the real nature of the tissue may be identified remains. In some adult fishes this is the ordinary condition of the hepatic organ, and without great care in the preparation of specimens, not a vestige of hepatic tissue will be discovered. In all these instances, however, the stages through which the gland-elementary part passes may be studied without difficulty, and specimens may be obtained which show every degree of alteration, from a transparent elementary part, completely destitute of fatty matter, to a body which appears to consist only of a huge oil-globule. It is surprising how large an accumulation of fat may occur in the liver in some of these cases. As much as 65·19 per cent. was found by one of us (L.S.B.) in one case, recorded by Dr. Budd.*

Of the removal of Adipose Tissue and the absorption of Fat.— Not less interesting than the consideration of the mode of development of adipose tissue is the question concerning the manner in which its removal is effected. It is well known that large quantities of fat which have been stored up in the body

* "Diseases of the Liver," 2nd ed., p. 284.

and have been collecting for a considerable time, may quickly disappear, in consequence of the fat being absorbed, and its elements applied to assist in the nutrition of tissues whose waste could not occur without consequences very damaging to the organism, and in maintaining the requisite temperature. The adipose tissue may, indeed, be regarded as a sort of storehouse, in which fat is accumulated as long as the body is abundantly supplied with food, from which it may be removed and appropriated, should a period of scarcity occur.

In the winter, when the fat of the fat bodies of the frog are being absorbed, the bioplasm of each vesicle can be seen spreading around the fatty matter, which gradually diminishes in amount in consequence of its conversion into bioplasm. On the distal side of the vesicle, phenomena of another kind are proceeding. The bioplasm is there undergoing change, and becoming resolved into substances, which are immediately taken up by the bioplasm of the blood and blood-vessels. As has been already described (p. 152), all nutritive operations are conducted through the intervention of bioplasm alone. As every kind of fatty material is formed from bioplasm, so its removal is effected only through the instrumentality of this living matter. It cannot be removed until it has been again taken up and converted into bioplasm. Moreover, the same bioplasm is instrumental in both operations:—in the one case taking certain constituents *from* the blood, increasing at their expense, and then undergoing conversion into fatty and other matters:—in the other, growing at the expense of this fatty matter already produced, and then becoming resolved into substances which find their way back again into the blood, and which are at length appropriated in part by other forms of bioplasm of the body. This view has been recently confirmed by Czajewicz, in some observations upon the adipose tissue of rabbits (Reichert and Du Bois Reymond's Archiv., 1866, p. 289).

In animals which have become rapidly emaciated, the fat cells of the adipose tissue are seen to be shrunken, and, instead of containing fatty matter, fluid, with some granules and one or two oil globules, are alone found. This interesting fact was first observed by Kölliker. The amount of fat in an individual vesicle may vary from time to time. The processes of forma-

tion and disintegration of the fat which has been already formed alternating with one another.

Abnormal Development of Adipose Tissue.—The uniform development of adipose tissue is sometimes disturbed, and in consequence of a circumscribed redundant growth, a tumour of enormous size may result. It is not uncommon to find this unusual growth springing from the subcutaneous adipose tissue of the limbs or trunk. In one particular spot the circumstances which determine the regular and even growth of the tissue are somehow altered, and growth having once burst its ordinary bounds, continues unceasingly, and often at an increasing rate, until a *tumour* of large size is produced. The structure of simple fatty tumours exactly accords with that of normal adipose tissue, and the arrangement of the capillary vessels is precisely the same. It is possible that the formation of these tumours may be due to the circumstance of a collection of bioplasm, which would under ordinary conditions, form a lobule of ordinary adipose tissue, being displaced at an early period of its development. Subjected to the influence of unusual conditions, the little lobule grows very quickly, and once but a germ, soon becomes developed into one of those, often huge, morbid growths.

Not only is the constantly growing fatty tumour like adipose tissue in its general characters, but in many instances the minute structure of the morbid growth could not be distinguished from that of the normal tissue.

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